

16.2.7. Adverse Event Listings (Each Subject)

Number	Title
Listing 16.2.7	Adverse Events

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Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / WORSENING NON-CARDIAC CHEST PAIN	28FEB2018 (1)	18APR2018 (50)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Flank pain / FLANK PAIN	04MAR2018 (5)	14MAR2018 (15)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	04MAR2018 (5)	22MAR2018 (23)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dysphonia / VOICE ALTERATION	04MAR2018 (5)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Syncope / SYNCOPE	11MAR2018 (12)	11MAR2018 (12)	Grade 3	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	04APR2018 (36)	11APR2018 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Sinus tachycardia / SINUS TACHYCARDIA	04APR2018 (36)	23APR2018 (55)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

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0101-0002	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	12APR2018 (44)	27APR2018 (59)	Grade 2	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Syncope / SYNCOPE	17APR2018 (49)	17APR2018 (49)	Grade 3	Resolved	Other: PATIENT HAD CT HEAD AND EKG	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	18APR2018 (50)	01MAY2018 (63)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	25APR2018 (57)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	28APR2018 (60)	09MAY2018 (71)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	29APR2018 (61)	16MAY2018 (78)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	02MAY2018 (64)	09MAY2018 (71)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0002	ADIPemPlatinum	Yes	Injury, poisoning and procedural complications / Fall / FALL	16MAY2018 (78)	16MAY2018 (78)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	16MAY2018 (78)	17MAY2018 (79)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	16MAY2018 (78)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	17MAY2018 (79)	23MAY2018 (85)	Grade 1	Resolved with Sequelae	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	23MAY2018 (85)		Grade 2	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Syncope / SYNCOPE	29MAY2018 (91)	29MAY2018 (91)	Grade 3	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	29MAY2018 (91)	30MAY2018 (92)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0002	ADIPemPlatinum	Yes	Cardiac disorders / Sinus tachycardia / SINUS TACHYCARDIA	29MAY2018 (91)	31MAY2018 (93)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	29MAY2018 (91)	31MAY2018 (93)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Nervous system disorders / Dizziness / DIZZINESS	29MAY2018 (91)	31MAY2018 (93)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	29MAY2018 (91)	31MAY2018 (93)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29MAY2018 (91)	06JUN2018 (99)	Grade 3	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	29MAY2018 (91)	06JUN2018 (99)	Grade 3	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Endocrine disorders / Adrenal insufficiency / ADRENAL INSUFFICIENCY	29MAY2018 (91)		Grade 2	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0002	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	06JUN2018 (99)	13JUN2018 (106)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	06JUN2018 (99)		Grade 2	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	14JUN2018 (107)	15JUN2018 (108)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Gait disturbance / GAIT DISTURBANCE	03JUL2018 (126)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	05JUL2018 (128)		Grade 2	Not Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0101-0003	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	03APR2018 (7)	05APR2018 (9)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Erythema / ERYTHEMA	03APR2018 (7)	15APR2018 (19)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0003	PlaceboPemPlatinum	Yes	Infections and infestations / Skin infection / SKIN INFECTION	03APR2018 (7)	28APR2018 (32)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed; Drug Interrupted / Dose Not Changed; Drug Interrupted / Not Applicable	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	04APR2018 (8)		Grade 2	Not Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Wound complication / WOUND COMPLICATION	04APR2018 (8)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Muscular weakness / GENERALIZED MUSCLE WEAKNESS	04APR2018 (8)		Grade 1	Not Resolved	Other: PATIENT ENCOURAGE D FOR PHYSICAL THERAPY WITH EXISTING VISITING NURSE SERVICE	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	11APR2018 (15)	07MAY2018 (41)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0003	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	11APR2018 (15)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Erythema / ERYTHEMA	15APR2018 (19)	28APR2018 (32)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	21APR2018 (25)	07MAY2018 (41)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	21APR2018 (25)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	01MAY2018 (35)	07MAY2018 (41)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
			Vascular disorders / Hypotension / HYPOTENSION	01MAY2018 (35)	07MAY2018 (41)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Urinary incontinence / URINARY INCONTINENCE	01MAY2018 (35)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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0101-0003	PlaceboPemPlatinum	Yes	Injury, poisoning and procedural complications / Fall / FALL	04MAY2018 (38)	04MAY2018 (38)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	04MAY2018 (38)	07MAY2018 (41)	Grade 4	Resolved	Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
			Blood and lymphatic system disorders / Anaemia / ANEMIA	07MAY2018 (41)		Grade 2	Not Resolved	None	Probably / Probably / Probably / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	07MAY2018 (41)		Grade 1	Not Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Wound complication / ERYTHEMA R CHEST WALL/WOUND	07MAY2018 (41)		Grade 1	Not Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	07MAY2018 (41)		Grade 3	Not Resolved	None	Probably / Probably / Probably / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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0101-0003	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	07MAY2018 (41)		Grade 2	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Rhinitis allergic / ALLERGIC RHINITIS	07MAY2018 (41)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
0101-0004	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	17MAY2018 (4)	20MAY2018 (7)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	18MAY2018 (5)	21MAY2018 (8)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	25MAY2018 (12)	26MAY2018 (13)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTAXIS	26MAY2018 (13)	26MAY2018 (13)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	30MAY2018 (17)	31MAY2018 (18)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0004	ADIPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	30MAY2018 (17)	04JUN2018 (22)	Grade 4	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	30MAY2018 (17)	04JUN2018 (22)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / ARTHRALGIA	30MAY2018 (17)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Urinary tract pain / URINARY TRACT PAIN	30MAY2018 (17)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	01JUN2018 (19)	01JUN2018 (19)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	01JUN2018 (19)	09JUN2018 (27)	Grade 1	Resolved	None	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02JUN2018 (20)	11JUN2018 (29)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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0101-0004	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Myalgia / MYALGIA	02JUN2018 (20)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	04JUN2018 (22)	11JUN2018 (29)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	04JUN2018 (22)	18JUN2018 (36)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11JUN2018 (29)	14AUG2018 (93)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	17JUN2018 (35)	20JUN2018 (38)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	17JUN2018 (35)	20JUN2018 (38)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	05JUL2018 (53)	16JUL2018 (64)	Grade 1	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0004	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	16JUL2018 (64)	17SEP2018 (127)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Alopecia / ALOPECIA	16JUL2018 (64)	15OCT2018 (155)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	02AUG2018 (81)	13AUG2018 (92)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Anxiety / ANXIETY	02AUG2018 (81)	12DEC2018 (213)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Depression / DEPRESSION	02AUG2018 (81)	12DEC2018 (213)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Insomnia / INSOMNIA	02AUG2018 (81)	12DEC2018 (213)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal distension / BLOATING	03AUG2018 (82)	13AUG2018 (92)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHEA	03AUG2018 (82)	13AUG2018 (92)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Periodontal disease / PERIODONTAL DISEASE	04AUG2018 (83)	19AUG2018 (98)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14AUG2018 (93)	27AUG2018 (106)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	14AUG2018 (93)	01OCT2018 (141)	Grade 1	Resolved	Medication	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	15AUG2018 (94)	17SEP2018 (127)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	20AUG2018 (99)	27AUG2018 (106)	Grade 3	Resolved with Sequelae	None	Possibly / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	27AUG2018 (106)	01OCT2018 (141)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0004	ADIPemPlatinum	Yes	Investigations / Platelet count decreased / PLATELET COUNT DECREASED	27AUG2018 (106)	12DEC2018 (213)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27AUG2018 (106)		Grade 1	Not Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness / DIZZINESS	04SEP2018 (114)	17SEP2018 (127)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	24SEP2018 (134)	01OCT2018 (141)	Grade 2	Resolved with Sequelae	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	01OCT2018 (141)	10OCT2018 (150)	Grade 3	Resolved	Medication	Probably / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY INFECTION	01OCT2018 (141)	15OCT2018 (155)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	10OCT2018 (150)	15OCT2018 (155)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0004	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / PAIN IN EXTREMITY SHOULDER	10OCT2018 (150)	29OCT2018 (169)	Grade 2	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	29OCT2018 (169)	13NOV2018 (184)	Grade 1	Resolved with Sequelae	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Cardiac disorders / Cardiac tamponade / PERICARDIAL TAMPONADE	21NOV2018 (192)	12DEC2018 (213)	Grade 4	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Cardiac disorders / Pericardial effusion / PERICARDIAL EFFUSION	21NOV2018 (192)	12DEC2018 (213)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0101-0006	PlaceboPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	10APR2019 (3)	15APR2019 (8)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	10APR2019 (3)	22APR2019 (15)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0006	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	10APR2019 (3)	26AUG2019 (141)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	11APR2019 (4)	14APR2019 (7)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	16APR2019 (9)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-POPULAR FACE	18APR2019 (11)	22APR2019 (15)	Grade 1	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Libido decreased / LIBIDO DECREASED	22APR2019 (15)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	24APR2019 (17)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	25APR2019 (18)	14JUN2019 (68)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Candida infection / THRUSH	06MAY2019 (29)	28MAY2019 (51)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	20MAY2019 (43)	22MAY2019 (45)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness / DIZZINESS	31MAY2019 (54)	02JUN2019 (56)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	05JUN2019 (59)	23JUN2019 (77)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	24JUN2019 (78)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	28JUN2019 (82)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Alopecia / ALOPECIA	03JUL2019 (87)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Oral candidiasis / ORAL THRUSH	17JUL2019 (101)	05AUG2019 (120)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	17JUL2019 (101)	12AUG2019 (127)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	21JUL2019 (105)	21JUL2019 (105)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	31JUL2019 (115)	04AUG2019 (119)	Grade 3	Resolved	Medication	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Skin infection / SKIN INFECTION, RIGHT WRIST	10AUG2019 (125)	26AUG2019 (141)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	12AUG2019 (127)	18AUG2019 (133)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Vascular disorders / Thrombophlebitis superficial / SUPERFICIAL THROMBOPHLEBITIS	12AUG2019 (127)	22SEP2019 (168)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Page 19 of 454

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0006	PlaceboPemPlatinum	Yes	Investigations / Blood creatinine increased / CREATININE INCREASED	19AUG2019 (134)	26AUG2019 (141)	Grade 2	Resolved	Medication	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	19AUG2019 (134)	22SEP2019 (168)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	04SEP2019 (150)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	23SEP2019 (169)	02OCT2019 (178)	Grade 1	Resolved	Other: PER SOURCE "CONTINUE TO FOLLOW CLOSELY".	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	23SEP2019 (169)		Grade 1	Ongoing	None	Unlikely / Probably / Unlikely / Unlikely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Reproductive system and breast disorders / Nipple disorder / NIPPLE DEFORMITY (NOS)	02OCT2019 (178)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Dizziness / DIZZINESS	16OCT2019 (192)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

^[2] Time (days) relative to date of first dose of study drug

[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0006	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	26OCT2019 (202)	27OCT2019 (203)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Campylobacter test positive / CAMPYLOBACTER POSITIVE	26OCT2019 (202)	27OCT2019 (203)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY INFECTION	26OCT2019 (202)	29OCT2019 (205)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Nervous system disorders / Dysgeusia / DYSGEUSIA	11NOV2019 (218)		Grade 2	Ongoing	Other: FOLLOW UP WITH LOCAL GI	Possibly / Possibly / Probably / Probably	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO POPULAR, LEFT BACK	06JAN2020 (274)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable	No
0101-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	17MAY2019 (5)	27MAY2019 (15)	Grade 1	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0008	ADIPemPlatinum	Yes	Ear and labyrinth disorders / Hypoacusis / HEARING IMPAIRED	22MAY2019 (10)		Grade 1	Ongoing	None	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER	24MAY2019 (12)	25MAY2019 (13)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	24MAY2019 (12)	26MAY2019 (14)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	24MAY2019 (12)	01JUN2019 (20)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	Yes
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	01JUN2019 (20)	02JUN2019 (21)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	06JUN2019 (25)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	08JUN2019 (27)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0008	ADIPemPlatinum	Yes	Immune system disorders / Anaphylactic reaction / ANAPHYLAXIS	18JUL2019 (67)	18JUL2019 (67)	Grade 4	Resolved	Medication; OXYGEN ADMINISTER ED VIA NC	Definitely / Unrelated / Unrelated / Unrelated	Drug Withdrawn / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
0101-0009	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	28JUN2019 (10)		Grade 2	Ongoing	None	Unlikely / Unlikely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	01JUL2019 (13)	06JUL2019 (18)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	07JUL2019 (19)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	12JUL2019 (24)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Depression / DEPRESSION	12JUL2019 (24)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13JUL2019 (25)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0009	ADIPemPlatinum	Yes	Gastrointestinal disorders / Stomatitis / MUCOSITIS, ORAL	17JUL2019 (29)	04AUG2019 (47)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly /	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed /	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	24JUL2019 (36)	31JUL2019 (43)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly /	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed /	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	31JUL2019 (43)	04AUG2019 (47)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely /	Unknown / Unknown / Not Applicable / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed /	No
			General disorders and administration site conditions / Oedema peripheral / EDEMA, LIMBS, BILATERAL LOWER EXTREMITY	01AUG2019 (44)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely /	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed /	No
			Injury, poisoning and procedural complications / Fall / FALL	02AUG2019 (45)	02AUG2019 (45)	Grade 2	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely /	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable /	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	05AUG2019 (48)	13AUG2019 (56)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly / Possibly /	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable /	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	05AUG2019 (48)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely / Unlikely /	Dose Not Changed / Not Applicable / Not Applicable / Dose Not Changed / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable / Not Applicable /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0009	ADIPemPlatinum	Yes	Nervous system disorders / Tremor / TREMOR	05AUG2019 (48)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	14AUG2019 (57)		Grade 3	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	14AUG2019 (57)		Grade 1	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Psychiatric disorders / Confusional state / CONFUSION	21AUG2019 (64)	23AUG2019 (66)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Eye disorders / Eyelid function disorder / EYELID FUNCTION DISORDER	21AUG2019 (64)	28AUG2019 (71)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0009	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	21AUG2019 (64)		Grade 3	Ongoing	Other: HOSPITALIZATION FOR THIS EVENT WAS DUE TO GRADE 1 CONFUSION, EYELID FUNCTION DISORDER	Unrelated / Unrelated / Unrelated / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS - BILATERAL LE EDEMA	21AUG2019 (64)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
0101-0010	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS - BILATERAL ANKLES	01AUG2019 (4)	03AUG2019 (6)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	01AUG2019 (4)	31OCT2019 (95)	Grade 2	Resolved	Medication	Unlikely / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dyspepsia / DYSPEPSIA GR. 2	01AUG2019 (4)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0010	PlaceboPemPlatinum	Yes	Nervous system disorders / Dysgeusia / DYSGEUSIA GRADE 1	05AUG2019 (8)	12SEP2019 (46)	Grade 1	Resolved with Sequelae	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	05AUG2019 (8)		Grade 1	Ongoing	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Insomnia / INSOMNIA	05AUG2019 (8)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	13AUG2019 (16)	25SEP2019 (59)	Grade 1	Resolved with Sequelae	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	20AUG2019 (23)	31OCT2019 (95)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Hypoacusis / HEARING IMPAIRED	25AUG2019 (28)		Grade 2	Ongoing	None	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Memory impairment / MEMORY IMPAIRMENT	27AUG2019 (30)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0010	PlaceboPemPlatinum	Yes	Nervous system disorders / Tremor / TREMOR	29AUG2019 (32)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS - TRACE TO LEFT ANKLE	10SEP2019 (44)	31OCT2019 (95)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	12SEP2019 (46)	17OCT2019 (81)	Grade 1	Resolved	None	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	12SEP2019 (46)		Grade 2	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	25SEP2019 (59)	07NOV2019 (102)	Grade 2	Resolved with Sequelae	None	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	10OCT2019 (74)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unlikely / Not Applicable	Drug Withdrawn / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Vascular disorders / Hypertension / HYPERTENSION	24OCT2019 (88)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0010	PlaceboPemPlatinum	Yes	Ear and labyrinth disorders / Tinnitus / TINNITUS	07NOV2019 (102)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0101-0011	ADIPemPlatinum	Yes	Gastrointestinal disorders / Gastroesophageal reflux disease / GASTROESOPHAGEAL REFLUX DISEASE	09SEP2019 (6)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / WORSENING DYSPNEA	11SEP2019 (8)		Grade 2	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Abdominal distension / BLOATING	16SEP2019 (13)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Pyrexia / FEVER	22SEP2019 (19)	22SEP2019 (19)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Withdrawn / Not Applicable	Yes
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	22SEP2019 (19)	25SEP2019 (22)	Grade 4	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Withdrawn / Not Applicable	Yes
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	23SEP2019 (20)	25SEP2019 (22)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Withdrawn / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0011	ADIPemPlatinum	Yes	Investigations / Platelet count decreased / PLATELET COUNT DECREASED	02OCT2019 (29)	07OCT2019 (34)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Possibly	Unknown / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	02OCT2019 (29)	09DEC2019 (97)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	07OCT2019 (34)	09OCT2019 (36)	Grade 3	Resolved	Other: STUDY DRUGS HELD	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Reproductive system and breast disorders / Scrotal pain / SCROTAL PAIN	21OCT2019 (48)	21NOV2019 (79)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Unlikely	Unknown / Unknown / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	21OCT2019 (48)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Possibly	Unknown / Unknown / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	01NOV2019 (59)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Vision blurred / BLURRED VISION -BILATERAL	04NOV2019 (62)		Grade 1	Ongoing	Other: OPHTHALMOLOGY CONSULT	Unlikely / Unlikely / Unlikely / Unlikely	Unknown / Unknown / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0101-0011	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	05NOV2019 (63)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY INFECTION	06DEC2019 (94)	22DEC2019 (110)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	09JAN2020 (128)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
0102-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	09SEP2017 (4)	09OCT2017 (34)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	09SEP2017 (4)	08OCT2018 (398)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Vertigo / VERTIGO	12SEP2017 (7)	13SEP2017 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	27SEP2017 (22)	04OCT2017 (29)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0001	ADIPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	27SEP2017 (22)	04OCT2017 (29)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	01OCT2017 (26)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	04OCT2017 (29)	18OCT2017 (43)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	18OCT2017 (43)	25OCT2017 (50)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	18OCT2017 (43)	29NOV2017 (85)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness / DIZZINESS	19OCT2017 (44)		Grade 1	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	25OCT2017 (50)	08NOV2017 (64)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0001	ADIPemPlatinum	Yes	Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	25OCT2017 (50)	15NOV2017 (71)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	25OCT2017 (50)		Grade 1	Ongoing	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALEMIA	27OCT2017 (52)	08NOV2017 (64)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypocalcaemia / HYPOCALCEMIA	29OCT2017 (54)	08NOV2017 (64)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoproteinaemia / HYPOPROTEINEMIA	30OCT2017 (55)	08NOV2017 (64)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	31OCT2017 (56)	29NOV2017 (85)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	15NOV2017 (71)	29NOV2017 (85)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0001	ADIPemPlatinum	Yes	Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	15NOV2017 (71)		Grade 2	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoproteinaemia / HYPOPROTEINEMIA	22NOV2017 (78)	29NOV2017 (85)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	22NOV2017 (78)		Grade 1	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypocalcaemia / HYPOCALCEMIA	22NOV2017 (78)		Grade 1	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29NOV2017 (85)	06DEC2017 (92)	Grade 3	Resolved	Surgical/ Diagnostic Procedure; Other: PRBC	Definitely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	06DEC2017 (92)	30DEC2017 (116)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	06DEC2017 (92)		Grade 2	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Chills / CHILLS	20DEC2017 (106)	29DEC2017 (115)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	20DEC2017 (106)	31DEC2017 (117)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Eye disorders / Vision blurred / BLURRED VISION	20DEC2017 (106)	02JAN2018 (119)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	20DEC2017 (106)	02JAN2018 (119)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Nervous system disorders / Ataxia / ATAXIA	20DEC2017 (106)	02JAN2018 (119)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	20DEC2017 (106)		Grade 3	Ongoing	None	Definitely /	Dose Not Changed /	No
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	21DEC2017 (107)	02JAN2018 (119)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated /	Dose Not Changed /	Yes
									Unrelated /	Dose Not Changed /	
									Unrelated /	Dose Not Changed /	
									Not Applicable	Not Applicable	

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	30DEC2017 (116)	21JAN2018 (138)	Grade 3	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	21JAN2018 (138)		Grade 2	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0002	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	31DEC2017 (5)	25APR2018 (120)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	17JAN2018 (22)	24JAN2018 (29)	Grade 4	Resolved	Other: DOSE DELAYED	Probably / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR	21FEB2018 (57)	25FEB2018 (61)	Grade 3	Resolved	None	Probably / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood urea increased / ELEVATED BUN	07MAR2018 (71)	14MAR2018 (78)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0002	ADIPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	14MAR2018 (78)	21MAR2018 (85)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSYPNEA	28MAR2018 (92)	28MAR2018 (92)	Grade 2	Resolved	Other: 2L OXYGEN GIVEN THROUGH NASAL ROUTE	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Skin and subcutaneous tissue disorders / Urticaria / URTICARIA	28MAR2018 (92)	28MAR2018 (92)	Grade 1	Resolved	Medication	Possibly / Possibly / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Interrupted / Not Applicable	No
			Vascular disorders / Flushing / FLUSHING	28MAR2018 (92)	28MAR2018 (92)	Grade 2	Resolved	Medication	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Interrupted / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	11APR2018 (106)	18APR2018 (113)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Nasal congestion / NASAL CONGESTION	18APR2018 (113)	18APR2018 (113)	Grade 2	Resolved	Medication	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Interrupted / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0002	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Pruritus / PRURITUS	18APR2018 (113)	18APR2018 (113)	Grade 1	Resolved	Medication	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Interrupted / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	09MAY2018 (134)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Nasopharyngitis / COMMON COLD	12JUL2018 (198)	18JUL2018 (204)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	18JUL2018 (204)	01AUG2018 (218)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Neck pain / NECK PAIN	05NOV2018 (314)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0003	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dysphonia / HOARSENESS	31JAN2018 (1)	03MAY2018 (93)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	08FEB2018 (9)	15FEB2018 (16)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0003	PlaceboPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	28FEB2018 (29)	16MAR2018 (45)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	28FEB2018 (29)	16MAR2018 (45)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	28FEB2018 (29)	03MAY2018 (93)	Grade 2	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	16MAR2018 (45)	03MAY2018 (93)	Grade 3	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	26MAR2018 (55)	27MAR2018 (56)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	28MAR2018 (57)	03MAY2018 (93)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	04APR2018 (64)	03MAY2018 (93)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0003	PlaceboPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	04APR2018 (64)	03MAY2018 (93)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	04APR2018 (64)	03MAY2018 (93)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood urea increased / ELEVATED BUN	16APR2018 (76)	03MAY2018 (93)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	17FEB2018 (5)	13JUL2018 (151)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	17FEB2018 (5)	13JUL2018 (151)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	21FEB2018 (9)	13JUL2018 (151)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0004	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	21FEB2018 (9)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	07MAR2018 (23)	18APR2018 (65)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	10MAR2018 (26)	13JUL2018 (151)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	10MAR2018 (26)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Pneumatosi / PNEUMATOSIS	21MAR2018 (37)		Grade 2	Resolving	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	21MAR2018 (37)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood urea increased / INCREASED BUN	29MAR2018 (45)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0004	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	18APR2018 (65)	13JUL2018 (151)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	18APR2018 (65)		Grade 2	Ongoing	Surgical/ Diagnostic Procedure	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / ELEVATED SERUM CREATININE	18APR2018 (65)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	25APR2018 (72)	25APR2018 (72)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	02MAY2018 (79)	13JUL2018 (151)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	18APR2018 (1)	23MAY2018 (36)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	25APR2018 (8)	02MAY2018 (15)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7 Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0005	PlaceboPemPlatinum	Yes	Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	16MAY2018 (29)	30MAY2018 (43)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	24MAY2018 (37)		Grade 2	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	30MAY2018 (43)	11JUL2018 (85)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	30MAY2018 (43)		Grade 2	Ongoing	None	Probably / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	06JUN2018 (50)	19JUN2018 (63)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	06JUN2018 (50)	19JUN2018 (63)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	19JUN2018 (63)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0005	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	05JUL2018 (79)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	11JUL2018 (85)	18JUL2018 (92)	Grade 3	Resolved	Other: TRANSFUSION	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELLS DECREASED	18JUL2018 (92)		Grade 1	Ongoing	None	Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Haematuria / HEMATURIA	20JUL2018 (94)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	30JUL2018 (104)		Grade 3	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0006	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	13JAN2019 (5)	27JAN2019 (19)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	13JAN2019 (5)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0006	PlaceboPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	16JAN2019 (8)	30JAN2019 (22)	Grade 1	Resolved	None	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	16JAN2019 (8)	30JAN2019 (22)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	16JAN2019 (8)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	20FEB2019 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	22JUL2019 (6)	25JUL2019 (9)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	07AUG2019 (22)	14AUG2019 (29)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dry mouth / DRY MOUTH	08AUG2019 (23)	14OCT2019 (90)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Vision blurred / BLURRED VISION	28AUG2019 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Muscle spasms / INTERMITTENT LEG CRAMPS	28AUG2019 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0008	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR	18SEP2019 (1)	20SEP2019 (3)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	25SEP2019 (8)	26SEP2019 (9)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	02OCT2019 (15)	14OCT2019 (27)	Grade 1	Resolved	None	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0008	PlaceboPemPlatinum	Yes	Investigations / Weight decreased / WEIGHT LOSS	02OCT2019 (15)	16OCT2019 (29)	Grade 1	Resolved	None	Definitely / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02OCT2019 (15)		Grade 2	Resolving	None	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	02OCT2019 (15)		Grade 2	Resolving	None	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	02OCT2019 (15)		Grade 1	Resolving	None	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR	04OCT2019 (17)		Grade 1	Resolving	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	09OCT2019 (22)		Grade 1	Resolving	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	12OCT2019 (25)	30OCT2019 (43)	Grade 2	Resolved	Medication	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0008	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	12OCT2019 (25)		Grade 2	Resolving	None	Definitely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	14OCT2019 (27)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	16OCT2019 (29)	30OCT2019 (43)	Grade 4	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	16OCT2019 (29)	30OCT2019 (43)	Grade 4	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Missing	No
			Investigations / Weight decreased / WEIGHT LOSS	16OCT2019 (29)		Grade 2	Resolving	None	Definitely / Definitely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Chronic kidney disease / CHRONIC KIDNEY DISEASE	30OCT2019 (43)	06NOV2019 (50)	Grade 2	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Withdrawn / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	30OCT2019 (43)		Grade 1	Resolving	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0008	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	06NOV2019 (50)		Grade 2	Resolving	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	06NOV2019 (50)		Grade 1	Resolving	None	Possibly / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	29NOV2019 (73)	30NOV2019 (74)	Grade 3	Resolved with	None	Unrelated / Unrelated / Unrelated / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Acute respiratory failure / ACUTE ON CHRONIC RESPIRATORY FAILURE	29NOV2019 (73)	03DEC2019 (77)	Grade 5	Fatal	None	Unrelated / Unrelated / Unrelated / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0102-0009	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	05OCT2019 (6)		Grade 1	Ongoing	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	05OCT2019 (6)		Grade 2	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0009	PlaceboPemPlatinum	Yes	Nervous system disorders / Neuropathy peripheral / NEUROPATHY	05OCT2019 (6)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	21OCT2019 (22)		Grade 1	Resolving	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09DEC2019 (71)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0102-0010	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	29JAN2020 (8)	08FEB2020 (18)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	29JAN2020 (8)	12FEB2020 (22)	Grade 1	Resolved	None	Unlikely / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	08FEB2020 (18)	12FEB2020 (22)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0010	ADIPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	12FEB2020 (22)		Grade 1	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY INFECTION	26FEB2020 (36)	03MAR2020 (42)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	01MAR2020 (40)	06MAR2020 (45)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	03MAR2020 (42)	05MAR2020 (44)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	03MAR2020 (42)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Dose Reduced; Drug Interrupted / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	05MAR2020 (44)	11MAR2020 (50)	Grade 3	Resolved	Other: 2 UNITS OF RBCS	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0010	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	11MAR2020 (50)	25MAR2020 (64)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCEMIA	11MAR2020 (50)	15APR2020 (85)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	18MAR2020 (57)	25MAR2020 (64)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	25MAR2020 (64)	01APR2020 (71)	Grade 3	Resolved	None	Unrelated /	Dose Not Changed /	No
			Nervous system disorders / Dizziness / DIZZINESS	13APR2020 (83)	15APR2020 (85)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	13APR2020 (83)	15APR2020 (85)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	14APR2020 (84)	15APR2020 (85)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0010	ADIPemPlatinum	Yes	Vascular disorders / Hypotension / HYPOTENSION	14APR2020 (84)	15APR2020 (85)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	14APR2020 (84)	20APR2020 (90)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	12MAY2020 (112)		Grade 3	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12MAY2020 (112)		Grade 2	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0102-0011	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	19MAR2020 (23)	25MAR2020 (29)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	19MAR2020 (23)	25MAR2020 (29)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Decubitus ulcer / BED SORES	19MAR2020 (23)	25MAR2020 (29)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0011	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	22MAR2020 (26)	24MAR2020 (28)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Drug Withdrawn / Not Applicable / Drug Withdrawn	Yes
0102-0012	ADIPemPlatinum	Yes	Investigations / Blood creatinine increased / CREATININE INCREASED	25MAR2020 (22)	01APR2020 (29)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	25MAR2020 (22)	01APR2020 (29)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	25MAR2020 (22)	01APR2020 (29)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	25MAR2020 (22)	22APR2020 (50)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	08APR2020 (36)	22APR2020 (50)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	14APR2020 (42)	15JUL2020 (134)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0012	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	22APR2020 (50)	26MAY2020 (84)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	06MAY2020 (64)	13MAY2020 (71)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	26MAY2020 (84)	03JUN2020 (92)	Grade 3	Resolved	Other: 1 UNIT OF PRBCS GIVEN	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	26MAY2020 (84)	03JUN2020 (92)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	26MAY2020 (84)		Grade 1	Resolving	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	03JUN2020 (92)	23JUN2020 (112)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	03JUN2020 (92)	09JUL2020 (128)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0012	ADIPemPlatinum	Yes	Investigations / Platelet count decreased / PLATELET COUNT DECREASED	16JUN2020 (105)	23JUN2020 (112)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09JUL2020 (128)	15JUL2020 (134)	Grade 3	Resolved	Other: PBRC	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	15JUL2020 (134)	06AUG2020 (156)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	15JUL2020 (134)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	29JUL2020 (148)	14AUG2020 (164)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0102-0013	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	11MAR2020 (1)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11MAR2020 (1)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0013	PlaceboPemPlatinum	Yes	Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	02APR2020 (23)	08APR2020 (29)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	02APR2020 (23)	24APR2020 (45)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	02APR2020 (23)	24APR2020 (45)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	08APR2020 (29)	24APR2020 (45)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	24APR2020 (45)	29APR2020 (50)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	24APR2020 (45)	13MAY2020 (64)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	24APR2020 (45)	13MAY2020 (64)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0013	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	13MAY2020 (64)	22MAY2020 (73)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	13MAY2020 (64)		Grade 3	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	13MAY2020 (64)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	13MAY2020 (64)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	22MAY2020 (73)		Grade 2	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	27MAY2020 (78)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	02JUN2020 (84)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0013	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	15JUN2020 (97)		Grade 3	Resolving	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0102-0014	ADIPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	19MAY2020 (23)	26MAY2020 (30)	Grade 3	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	19MAY2020 (23)		Grade 1	Ongoing	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	11JUN2020 (46)	15JUN2020 (50)	Grade 3	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	11JUN2020 (46)	15JUN2020 (50)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	15JUN2020 (50)	30JUN2020 (65)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	15JUN2020 (50)	30JUN2020 (65)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0014	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCEMIA	15JUN2020 (50)	30JUN2020 (65)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	15JUN2020 (50)	30JUN2020 (65)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	30JUN2020 (65)	06JUL2020 (71)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	30JUN2020 (65)	06JUL2020 (71)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	20JUL2020 (85)	27JUL2020 (92)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	20JUL2020 (85)	27JUL2020 (92)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	27JUL2020 (92)	10AUG2020 (106)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Drug Interrupted / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0014	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	17AUG2020 (113)	26AUG2020 (122)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	27AUG2020 (123)	28AUG2020 (124)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	Yes
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO PAPULAR	08SEP2020 (135)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	28SEP2020 (155)	25JAN2021 (274)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	28SEP2020 (155)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	09FEB2021 (289)	10FEB2021 (290)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0102-0015	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	21JUL2020 (1)	11AUG2020 (22)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0015	ADIPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	21JUL2020 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCEMIA	21JUL2020 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	25JUL2020 (5)		Grade 2	Resolving	None	Unrelated / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Confusional state / CONFUSION	26JUL2020 (6)	28JUL2020 (8)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	11AUG2020 (22)		Grade 2	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	11AUG2020 (22)		Grade 1	Resolving	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	11AUG2020 (22)		Grade 1	Ongoing	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0102-0015	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	02SEP2020 (44)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	02SEP2020 (44)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	22SEP2020 (64)		Grade 3	Resolving	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / PAIN (UPPER AND LOWER RIGHT LUNG)	24SEP2020 (66)		Grade 1	Not Resolved	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	26SEP2020 (68)		Grade 4	Resolving	Hospitalization/ Prolonged Hospitalization	Unrelated /	Drug Withdrawn /	Yes
0103-0001	ADIPemPlatinum	Yes	Cardiac disorders / Cardiac arrest / CARDIAC ARREST	12SEP2017 (7)	14SEP2017 (9)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated /	Drug Interrupted; Drug Withdrawn /	Yes

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	10MAR2018 (4)	20MAR2018 (14)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Pleural effusion / PLEURAL EFFUSION	29MAR2018 (23)	01APR2018 (26)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Investigations / Neutrophil count increased / NEUTROPHIL COUNT INCREASE	25APR2018 (50)	01MAY2018 (56)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Not Applicable	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	25APR2018 (50)	02MAY2018 (57)	Grade 3	Resolved	None	Unrelated / Possibly / Not Applicable / Not Applicable	Dose Not Changed / Drug Interrupted / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTASIS	25APR2018 (50)	09MAY2018 (64)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Drug Interrupted / Drug Interrupted / Not Applicable / Not Applicable	No
			Investigations / Neutrophil count increased / NEUTROPHIL COUNT INCREASE	01MAY2018 (56)	07MAY2018 (62)	Grade 3	Resolved	Medication	Unrelated / Probably / Not Applicable / Not Applicable	Drug Interrupted / Drug Interrupted / Not Applicable / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	01MAY2018 (56)	09MAY2018 (64)	Grade 3	Resolved	None	Unrelated / Probably / Not Applicable / Not Applicable	Dose Not Changed / Drug Interrupted / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0003	ADIPemPlatinum	Yes	Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	02MAY2018 (57)	07MAY2018 (62)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Not Applicable	Dose Not Changed / Drug Interrupted / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Joint swelling / SWELLING BOTH ANKLES	16MAY2018 (71)	20JUN2018 (106)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	26JUN2018 (112)	17JUL2018 (133)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	26JUN2018 (112)	17JUL2018 (133)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	26JUN2018 (112)	07AUG2018 (154)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Reproductive system and breast disorders / Vaginal haemorrhage / VAGINAL HEMORRHAGE	05JUL2018 (121)	07JUL2018 (123)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	05JUL2018 (121)	02AUG2018 (149)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0003	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	17JUL2018 (133)	14AUG2018 (161)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	17JUL2018 (133)	29AUG2018 (176)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASED	02AUG2018 (149)		Grade 1	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Aspartate aminotransferase increased / ASPARTATE AMINOTRANSFERASE INCREASED	14AUG2018 (161)	02OCT2018 (210)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29AUG2018 (176)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	25SEP2018 (203)		Grade 1	Not Resolved	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0005	ADIPemPlatinum	Yes	Infections and infestations / Septic shock / SEPSIS SHOCK	19MAY2018 (6)		Grade 4	Ongoing	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
0103-0006	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH ON HEAD	16JUN2018 (3)	27JUN2018 (14)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	10AUG2018 (58)	12AUG2018 (60)	Grade 2	Resolved	None	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	06SEP2018 (85)	06SEP2018 (85)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS	09SEP2018 (88)	13SEP2018 (92)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON NECK	16SEP2018 (95)	27SEP2018 (106)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Painful respiration / PAINFUL BREATHING	16SEP2018 (95)	26OCT2018 (135)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0006	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Axillary pain / PAIN UNDER RIGHT ARM PIT	29SEP2018 (108)	26OCT2018 (135)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON- CARDIAC CHEST PAIN	29SEP2018 (108)	26OCT2018 (135)	Grade 3	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0103-0009	ADIPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHEA	21AUG2019 (8)	23AUG2019 (10)	Grade 2	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus generalised / ITCHINESS	28AUG2019 (15)	08SEP2019 (26)	Grade 1	Resolved	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON BUTTOCKS	29AUG2019 (16)	30AUG2019 (17)	Grade 1	Resolved	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / INTERMITTENT COUGH	30AUG2019 (17)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON BOTH LEGS	04SEP2019 (22)	08SEP2019 (26)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0009	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	05SEP2019 (23)		Grade 2	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	01OCT2019 (49)	30OCT2019 (78)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	03OCT2019 (51)	30OCT2019 (78)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	12NOV2019 (91)	17DEC2019 (126)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0103-0010	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Chills / INTERMITTENT BODY CHILLS	25MAY2020 (1)	27MAY2020 (3)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	29MAY2020 (5)	01JUN2020 (8)	Grade 1	Resolved	None	Unrelated / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0010	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	02JUN2020 (9)	08JUN2020 (15)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	15JUN2020 (22)	12JUL2020 (49)	Grade 1	Resolved	Surgical/ Diagnostic Procedure	Possibly / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Weight decreased / WEIGHT LOSS	06JUL2020 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASE APPETITE	06JUL2020 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Vomiting / INTERMITTENT VOMITING	12JUL2020 (49)	14OCT2020 (143)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Blindness transient / TEMPORARY VISION LOSS	23JUL2020 (60)	23JUL2020 (60)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Eye disorders / Diplopia / DOUBLE VISION	23JUL2020 (60)	23JUL2020 (60)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0103-0010	PlaceboPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	28JUL2020 (65)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / INCREASE LEFT POSTERIOR CHEST WALL PAIN	24AUG2020 (92)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Peripheral swelling / LEG SWELLING	04NOV2020 (164)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SOB	04NOV2020 (164)		Grade 1	Not Resolved	None	Possibly / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Sedation / OVER SEDATIVE	03DEC2020 (193)	09DEC2020 (199)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17DEC2020 (207)		Grade 3	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	26DEC2020 (216)	28DEC2020 (218)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Not Applicable / Not Applicable / Missing	Yes

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Stomatitis / STOMATITIS, INTERMITTENT	16APR2018 (6)	29MAY2018 (49)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	16APR2018 (6)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	23APR2018 (13)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	30APR2018 (20)	07MAY2018 (27)	Grade 1	Resolved	Medication	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypertension / HYPERTENSION, WORSENING	30APR2018 (20)	07MAY2018 (27)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	05MAY2018 (25)	21MAY2018 (41)	Grade 4	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	07MAY2018 (27)	21MAY2018 (41)	Grade 2	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0001	PlaceboPemPlatinum	Yes	Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	07MAY2018 (27)	21MAY2018 (41)	Grade 3	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	07MAY2018 (27)	21MAY2018 (41)	Grade 4	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	21MAY2018 (41)	11JUN2018 (62)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	21MAY2018 (41)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / STOMATITIS	29MAY2018 (49)	11JUN2018 (62)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / LYMPHOCYTE COUNT DECREASED	29MAY2018 (49)	11JUN2018 (62)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	29MAY2018 (49)	11JUN2018 (62)	Grade 4	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0001	PlaceboPemPlatinum	Yes	Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	29MAY2018 (49)	11JUN2018 (62)	Grade 4	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	11JUN2018 (62)	18JUN2018 (69)	Grade 3	Resolved	Other: 2 UNITS PRBCS	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			General disorders and administration site conditions / Gait disturbance / GAIT DISTURBANCE	11JUN2018 (62)	18JUN2018 (69)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Unknown	No
			General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS	11JUN2018 (62)	18JUN2018 (69)	Grade 1	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	11JUN2018 (62)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11JUN2018 (62)		Grade 2	Not Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / RIGHT-SIDED CHEST WALL PAIN, WORSENING	18JUN2018 (69)		Grade 3	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0003	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal distension / BLOATING	13FEB2019 (22)	05APR2019 (73)	Grade 1	Resolved	None	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	13FEB2019 (22)	05APR2019 (73)	Grade 1	Resolved	Medication	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / GASTROESOPHAGEAL REFLUX DISEASE	13FEB2019 (22)	05APR2019 (73)	Grade 2	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13FEB2019 (22)	05APR2019 (73)	Grade 1	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	13FEB2019 (22)	05APR2019 (73)	Grade 2	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13FEB2019 (22)		Grade 1	Not Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Embolism / THROMBOEMBOLIC EVENT RIGHT LOWER EXTREMITY	21FEB2019 (30)	06MAR2019 (43)	Grade 4	Resolved	Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	08JUL2019 (22)	08JUL2019 (22)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	08JUL2019 (22)	15JUL2019 (29)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	08JUL2019 (22)	15JUL2019 (29)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	08JUL2019 (22)	15JUL2019 (29)	Grade 3	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	15JUL2019 (29)	22JUL2019 (36)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	27JUL2019 (41)	19AUG2019 (64)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA, INTERMITTENT	19AUG2019 (64)		Grade 1	Not Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0004	ADIPemPlatinum	Yes	Infections and infestations / Folliculitis / FOLLICULITIS	26AUG2019 (71)	09SEP2019 (85)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	26AUG2019 (71)	09SEP2019 (85)	Grade 3	Resolved	None	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	26AUG2019 (71)	09SEP2019 (85)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Embolism / THROMBOEMBOLIC EVENT	03SEP2019 (79)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA, INTERMITTENT	09SEP2019 (85)	11NOV2019 (148)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	16SEP2019 (92)	30SEP2019 (106)	Grade 3	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	30SEP2019 (106)	21OCT2019 (127)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0004	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION, INTERMITTENT	30SEP2019 (106)	11NOV2019 (148)	Grade 2	Resolved	None	Possibly /	Dose Not Changed /	No
			Renal and urinary disorders / Pollakiuria / URINARY FREQUENCY	30SEP2019 (106)	02DEC2019 (169)	Grade 1	Resolved	None	Possibly /	Dose Not Changed /	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	21OCT2019 (127)	11NOV2019 (148)	Grade 3	Resolved	None	Not Applicable	Dose Not Changed /	No
			Vascular disorders / Hypertension / HYPERTENSION	11NOV2019 (148)	18NOV2019 (155)	Grade 3	Resolved	None	Possibly /	Dose Not Changed /	No
			Vascular disorders / Hypertension / HYPERTENSION	18NOV2019 (155)		Grade 2	Not Resolved	None	Unrelated /	Not Applicable /	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	02DEC2019 (169)	09DEC2019 (176)	Grade 3	Resolved	None	Possibly /	Dose Not Changed /	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	02DEC2019 (169)	31DEC2019 (198)	Grade 3	Resolved	None	Definitely /	Drug Interrupted /	No
									Unrelated /	Not Applicable /	
									Unrelated /	Not Applicable /	
									Possibly /	Dose Not Changed /	No
									Possibly /	Not Applicable /	
									Possibly /	Not Applicable /	
									Not Applicable	Not Applicable	

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION, INTERMITTENT	02DEC2019 (169)		Grade 1	Not Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Paraesthesia / PARESTHESIA LEFT BREAST	31DEC2019 (198)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0104-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	16NOV2019 (13)	25NOV2019 (22)	Grade 3	Resolved	Medication	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	18NOV2019 (15)	25NOV2019 (22)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	18NOV2019 (15)	02DEC2019 (29)	Grade 1	Resolved	None	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	25NOV2019 (22)	02DEC2019 (29)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted; Drug Withdrawn / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0006	ADIPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	25NOV2019 (22)	02DEC2019 (29)	Grade 3	Resolved	None	Probably / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	25NOV2019 (22)	09DEC2019 (36)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	25NOV2019 (22)	09DEC2019 (36)	Grade 1	Resolved	Medication	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	25NOV2019 (22)	09DEC2019 (36)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	25NOV2019 (22)	17FEB2020 (106)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE, INTERMITTENT	02DEC2019 (29)	24FEB2020 (113)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Unlikely	Drug Interrupted / Drug Interrupted / Dose Not Changed / Drug Interrupted	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09DEC2019 (36)	31DEC2019 (58)	Grade 3	Resolved	Other: TRANSFUSION	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0006	ADIPemPlatinum	Yes	Investigations / Haematocrit decreased / HEMATOCRIT DECREASED	16DEC2019 (43)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Red blood cell count decreased / RED BLOOD CELL DECREASED	16DEC2019 (43)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23DEC2019 (50)	31DEC2019 (58)	Grade 2	Resolved	None	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31DEC2019 (58)	20JAN2020 (78)	Grade 1	Resolved	None	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Weight decreased / WEIGHT LOSS	31DEC2019 (58)	13APR2020 (162)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Immune system disorders / Hypersensitivity / ALLERGIC REACTION	06JAN2020 (64)	13JAN2020 (71)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	20JAN2020 (78)	10FEB2020 (99)	Grade 3	Resolved	None	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	20JAN2020 (78)	17FEB2020 (106)	Grade 2	Resolved	None	Probably /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	10FEB2020 (99)	17FEB2020 (106)	Grade 1	Resolved	None	Probably /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17FEB2020 (106)		Grade 1	Not Resolved	None	Probably /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	02MAR2020 (120)		Grade 1	Not Resolved	None	Probably /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	16MAR2020 (134)	06APR2020 (155)	Grade 3	Resolved	Other: 2 UNITS PRBCS	Probably /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	30MAR2020 (148)		Grade 1	Not Resolved	None	Probably /	Dose Not Changed /	No
			Investigations / Weight decreased / WEIGHT LOSS	13APR2020 (162)		Grade 2	Not Resolved	None	Probably /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0104-0006	ADIPemPlatinum	Yes	Neoplasms benign, malignant and unspecified (incl cysts and polyps) / Tumour pain / TUMOR PAIN	13APR2020 (162)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0107-0001	ADIPemPlatinum	Yes	Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	01MAY2018 (22)	06MAY2018 (27)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL DECREASED	07MAY2018 (28)	27AUG2019 (505)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	18MAY2018 (39)	18MAY2018 (39)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness / DIZZINESS	29MAY2018 (50)	31JAN2020 (662)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Vascular disorders / Hypotension / HYPOTENSION	29MAY2018 (50)	31JAN2020 (662)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	19JUN2018 (71)	31JAN2020 (662)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	30AUG2018 (9)	01DEC2018 (102)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13SEP2018 (23)	20SEP2018 (30)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	25OCT2018 (65)	25OCT2018 (65)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	15NOV2018 (86)	15NOV2018 (86)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER	07FEB2019 (170)	07FEB2019 (170)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	04APR2019 (226)	04APR2019 (226)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Lentigo / LENTIGO	05APR2019 (227)	08JAN2020 (505)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	10OCT2019 (415)	17OCT2019 (422)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	10OCT2019 (415)	09JUN2021 (1023)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0107-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Flatulence / FLATULENCE	27DEC2018 (10)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Hyperchlorhydria / HYPERACIDITY	27DEC2018 (10)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LOWER BACK PAIN	08JAN2019 (22)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19JAN2019 (33)		Grade 1	Not Resolved	None	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Sinus tachycardia / SINUS TACHYCARDIA	29JAN2019 (43)		Grade 1	Not Resolved	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC PRESSURE TO RIGHT UPPER CHEST	07FEB2019 (52)	05MAR2019 (78)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Influenza like illness / FLU-LIKE SYMPTOMS	08FEB2019 (53)	10FEB2019 (55)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	27FEB2019 (72)	27FEB2019 (72)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC RIGHT SIDED CHEST PAIN	06MAR2019 (79)		Grade 3	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	14MAR2019 (87)		Grade 1	Not Resolved	None	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	14MAR2019 (87)		Grade 1	Not Resolved	None	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	27MAR2019 (100)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0107-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / LOW GRADE FEVER	19FEB2019 (1)	19FEB2019 (1)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY INFECTION	04MAR2019 (14)	05APR2019 (46)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	12MAR2019 (22)	04APR2019 (45)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / DYSPNEA ON EXERTION	05APR2019 (46)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01JUN2019 (103)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Missing / Missing	No
			Nervous system disorders / Dizziness / DIZZINESS	04JUN2019 (106)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	01JUL2019 (133)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Hyperhidrosis / HYPERHYDROSIS IN BACK	23JUL2019 (155)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST DISCOMFORT	13AUG2019 (176)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Arthralgia / RIGHT HIP PAIN	06SEP2019 (200)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / LEFT SIDE PAIN WHEN COUGHING	08OCT2019 (232)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
0107-0006	ADIPemPlatinum	Yes	Investigations / Glomerular filtration rate decreased / LOW GFR	15MAR2019 (3)	13AUG2019 (154)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Chills / RIGORS	27MAR2019 (15)	27MAR2019 (15)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	08APR2019 (27)	13AUG2019 (154)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	09APR2019 (28)	09APR2019 (28)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Leukocytosis / LEUKOCYTOSIS	09APR2019 (28)	14MAY2019 (63)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	09MAY2019 (58)	09MAY2019 (58)	Grade 1	Resolved	Medication	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Tremor / SHAKING	09MAY2019 (58)	09MAY2019 (58)	Grade 1	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	10MAY2019 (59)	13AUG2019 (154)	Grade 2	Resolved	None	Unrelated / Possibly / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	10MAY2019 (59)	13AUG2019 (154)	Grade 2	Resolved	None	Unrelated / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Haemoglobin decreased / LOW HEMOGLOBIN	15MAY2019 (64)	16MAY2019 (65)	Grade 2	Resolved	Other: TREATED WITH PACKED RED BLOOD CELLS	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	27MAY2019 (76)	13AUG2019 (154)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Urinary retention / URINARY RETENTION	05JUN2019 (85)	13AUG2019 (154)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Orthostatic hypotension / ORTHOSTASIS	18JUN2019 (98)	18JUN2019 (98)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Haematuria / HEMATURIA	18JUN2019 (98)	26JUN2019 (106)	Grade 1	Resolved	Other: TURP PROCEDURE	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0006	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	18JUN2019 (98)	26JUL2019 (136)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / WEAKNESS	02JUL2019 (112)	13AUG2019 (154)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Non-cardiac chest pain / PAIN IN CHEST -NON-CARDIAC	02JUL2019 (112)	13AUG2019 (154)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	02JUL2019 (112)	13AUG2019 (154)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Investigations / Weight decreased / WEIGHT LOSS	03JUL2019 (113)	13AUG2019 (154)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Renal and urinary disorders / Urinary retention / URINARY RETENTION	09APR2022 (1124)	09APR2022 (1124)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0007	ADIPemPlatinum	Yes	Investigations / Haemoglobin decreased / LOW HEMOGLOBIN	29OCT2019 (9)	07NOV2019 (18)	Grade 2	Resolved	None	Definitely / Definitely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	04NOV2019 (15)	07NOV2019 (18)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Injury, poisoning and procedural complications / Fall / FALL	07NOV2019 (18)	07NOV2019 (18)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	07NOV2019 (18)	13NOV2019 (24)	Grade 3	Resolved	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	Yes
			Blood and lymphatic system disorders / Pancytopenia / PANCYTOPENIA	08NOV2019 (19)	11NOV2019 (22)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	10NOV2019 (21)	01JAN2020 (73)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0007	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Normochromic normocytic anaemia / NORMOCYTIC ANEMIA	12NOV2019 (23)	28NOV2019 (39)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Vascular disorders / Orthostatic hypotension / ORTHOSTATIC HYPOTENSION	13NOV2019 (24)	28NOV2019 (39)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	20NOV2019 (31)	28NOV2019 (39)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Investigations / Haemoglobin decreased / LOW HEMOGLOBIN	20NOV2019 (31)		Grade 2	Not Resolved	None	Definitely / Definitely / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
0107-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	01NOV2019 (4)	14JAN2020 (78)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Flatulence / FLATULENCE	01NOV2019 (4)	15SEP2020 (323)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0008	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19NOV2019 (22)	26NOV2019 (29)	Grade 2	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	03DEC2019 (36)	08SEP2020 (316)	Grade 2	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	17DEC2019 (50)	28JAN2020 (92)	Grade 2	Resolved	Other: 2 UNITS OF PRBC'S GIVEN	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Withdrawn / Dose Reduced / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17DEC2019 (50)	15SEP2020 (323)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	14JAN2020 (78)	16JAN2020 (80)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	14JAN2020 (78)	16JAN2020 (80)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH-INTERMITTENT	14JAN2020 (78)	28JUN2020 (244)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0008	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	14JAN2020 (78)	15SEP2020 (323)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	21JAN2020 (85)	28JAN2020 (92)	Grade 3	Resolved	Other: PLATELET TRANSFUSION	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	No
			Psychiatric disorders / Confusional state / CONFUSION	21JAN2020 (85)	15SEP2020 (323)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	30JAN2020 (94)	03FEB2020 (98)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Drug Withdrawn / Missing	Yes
			Vascular disorders / Lymphoedema / LYMPHEDEMA	06FEB2020 (101)	15SEP2020 (323)	Grade 1	Resolved	None	Unrelated / Not Applicable / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Psychiatric disorders / Anxiety / ANXIETY	07FEB2020 (102)	15SEP2020 (323)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	09FEB2020 (104)	11FEB2020 (106)	Grade 2	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization	Unlikely / Unrelated / Definitely / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Missing	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Gastroesophageal reflux disease / ACID REFLUX	11FEB2020 (106)	15SEP2020 (323)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Ear and labyrinth disorders / Deafness / HEARING LOSS	20FEB2020 (115)	15SEP2020 (323)	Grade 2	Resolved	None	Probably / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	11MAR2020 (135)	11MAR2020 (135)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Blood uric acid increased / ELEVATED URIC ACID	12MAR2020 (136)	15SEP2020 (323)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / ITCHING	12MAR2020 (136)	15SEP2020 (323)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Psychiatric disorders / Anxiety / WORSENING ANXIETY	23APR2020 (178)	15SEP2020 (323)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	20MAY2020 (205)	20MAY2020 (205)	Grade 2	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0008	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Flank pain / RIGHT FLANK PAIN	27MAY2020 (212)	15SEP2020 (323)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / International normalised ratio increased / ELEVATED INR	25JUN2020 (241)	15SEP2020 (323)	Grade 2	Resolved	None	Definitely / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Prothrombin time prolonged / ELEVATED PT	25JUN2020 (241)	15SEP2020 (323)	Grade 2	Resolved	None	Definitely / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	29JUN2020 (245)	01JUL2020 (247)	Grade 3	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Bacterial infection / BACTERIAL INFECTION	29JUN2020 (245)	26AUG2020 (303)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Sepsis / SEVERE SEPSIS	26JUL2020 (272)	29JUL2020 (275)	Grade 3	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Psychiatric disorders / Mental status changes / ALTERED MENTAL STATUS	26JUL2020 (272)	15SEP2020 (323)	Grade 3	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0008	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	20AUG2020 (297)	15SEP2020 (323)	Grade 3	Resolved	None	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable	No
0107-0010	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	02DEC2019 (8)	01APR2021 (494)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / INCREASED PLEURAL PAIN	16DEC2019 (22)	01APR2021 (494)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Pruritus / ITCHING	16DEC2019 (22)	01APR2021 (494)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	23DEC2019 (29)	06JAN2020 (43)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Arthralgia / PAIN IN LEFT HIP	23DEC2019 (29)	01APR2021 (494)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Neuropathy peripheral / MILD NEUROPATHY IN TOES AND FINGERS	23DEC2019 (29)	01APR2021 (494)	Grade 1	Resolved	Medication	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0010	PlaceboPemPlatinum	Yes	Psychiatric disorders / Irritability / IRRITABILITY	23DEC2019 (29)	01APR2021 (494)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / REFLUX	27DEC2019 (33)	01APR2021 (494)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Headache / HEADACHE	27DEC2019 (33)	01APR2021 (494)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	06JAN2020 (43)	01APR2021 (494)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Sinus congestion / SINUS CONGESTION	13JAN2020 (50)	01APR2021 (494)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Cardiac disorders / Palpitations / HEART PALPITATION	29MAR2020 (126)	29MAR2020 (126)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Blood pressure increased / ELEVATED BLOOD PRESSURE	30MAR2020 (127)	13APR2020 (141)	Grade 2	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0107-0010	PlaceboPemPlatinum	Yes	Nervous system disorders / Dizziness / DIZZINESS	11MAY2020 (169)	01APR2021 (494)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
0107-0011	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Gastroesophageal reflux disease / GASTROESOPHAGEAL REFLUX DISEASE	07JUN2020 (7)	06SEP2020 (98)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	17JUN2020 (17)	06SEP2020 (98)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Vomiting / VOMITING	17JUN2020 (17)	06SEP2020 (98)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	22JUN2020 (22)	06SEP2020 (98)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / LEFT SHOULDER PAIN	13JUL2020 (43)	06SEP2020 (98)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	30JAN2019 (1)	06FEB2019 (8)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Pollakiuria / URINARY FREQUENCY	01FEB2019 (3)	06FEB2019 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13FEB2019 (15)	14FEB2019 (16)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Confusional state / CONFUSION	13FEB2019 (15)	14FEB2019 (16)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN (WORSENING)	13FEB2019 (15)	27FEB2019 (29)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE (WORSENING)	13FEB2019 (15)	14MAR2019 (44)	Grade 2	Resolved	Other: CISPLATIN DOSE REDUCTION	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGUESIA	13FEB2019 (15)	14MAR2019 (44)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0002	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	28FEB2019 (30)	03MAR2019 (33)	Grade 3	Resolved	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	05MAR2019 (35)	06MAR2019 (36)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
0108-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	15MAR2019 (3)	19MAR2019 (7)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20MAR2019 (8)	26MAR2019 (14)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Axillary pain / L AXILLARY PAIN	20MAR2019 (8)	02APR2019 (21)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / R CHEST PAIN (NON-CARDIAC)	20MAR2019 (8)	02APR2019 (21)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0003	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / L CHEST WALL PAIN	20MAR2019 (8)	02APR2019 (21)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	20MAR2019 (8)		Grade 2	Unknown	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / RIGHT-SIDED PULMONARY EMBOLISM	20MAR2019 (8)		Grade 3	Unknown	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27MAR2019 (15)	22APR2019 (41)	Grade 1	Resolved	None	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	27MAR2019 (15)		Grade 1	Not Resolved	None	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Depression / DEPRESSION	27MAR2019 (15)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Unresponsive to stimuli / EPISODE OF UNRESPONSIVENESS	03APR2019 (22)	03APR2019 (22)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0003	ADIPemPlatinum	Yes	General disorders and administration site conditions / Axillary pain / LEFT AXILLARY PAIN	03APR2019 (22)		Grade 1	Unknown	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / LEFT CHEST WALL PAIN	03APR2019 (22)		Grade 1	Unknown	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	07APR2019 (26)		Grade 1	Not Resolved	Medication	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dysphagia / DYSPHAGIA	10APR2019 (29)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	10APR2019 (29)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	23APR2019 (42)	23APR2019 (42)	Grade 2	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23APR2019 (42)		Grade 2	Not Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0003	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	23APR2019 (42)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	24APR2019 (43)	06MAY2019 (55)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0108-0004	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	01MAY2019 (1)	28MAY2019 (28)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	01MAY2019 (1)	04JUN2019 (35)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	01MAY2019 (1)	05JUN2019 (36)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	01MAY2019 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / DYSPNEA ON EXERTION	01MAY2019 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	08MAY2019 (8)	15MAY2019 (15)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	08MAY2019 (8)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	08MAY2019 (8)		Grade 1	Not Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	15MAY2019 (15)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Anxiety / ANXIETY	15MAY2019 (15)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERCALEMIA	22MAY2019 (22)	28MAY2019 (28)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERCALEMIA	29MAY2019 (29)	05JUN2019 (36)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	29MAY2019 (29)		Grade 1	Not Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	29MAY2019 (29)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Muscle twitching / TWITCHING IN BILATERAL HANDS	29MAY2019 (29)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	05JUN2019 (36)	05JUN2019 (36)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	05JUN2019 (36)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / INTERMITTENT NEUROPATHY	05JUN2019 (36)		Grade 1	Ongoing	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Urinary incontinence / URINARY INCONTINENCE	05JUN2019 (36)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0004	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERCALEMIA	06JUN2019 (37)	06JUN2019 (37)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	06JUN2019 (37)	19JUN2019 (50)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERCALEMIA	07JUN2019 (38)	07JUN2019 (38)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Posterior reversible encephalopathy syndrome / POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME	22JUN2019 (53)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0108-0006	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / LEFT SHOULDER PAIN	01NOV2019 (3)	01NOV2019 (3)	Grade 1	Resolved	Other: HEAT PACK	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01NOV2019 (3)	19NOV2019 (21)	Grade 1	Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0006	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	01NOV2019 (3)	20NOV2019 (22)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dyspepsia / HEARTBURN	02NOV2019 (4)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20NOV2019 (22)	03DEC2019 (35)	Grade 2	Resolved	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	04DEC2019 (36)		Grade 1	Not Resolved	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / UPPER BACK PAIN	04DEC2019 (36)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Pain in extremity / UNDER ARM PAIN	04DEC2019 (36)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood thyroid stimulating hormone increased / THYROID STIMULATING HORMONE INCREASED	30DEC2019 (62)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0006	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / POSTERIOR CHEST WALL MASS PAIN	30DEC2019 (62)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Memory impairment / DIFFICULTY WITH MEMORY	30DEC2019 (62)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Tremor / SHAKINESS	30DEC2019 (62)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
0108-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	05FEB2020 (1)	12FEB2020 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / INTERMITTENT FATIGUE	05FEB2020 (1)	27FEB2020 (23)	Grade 1	Resolved	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	10FEB2020 (6)	12FEB2020 (8)	Grade 1	Resolved	Medication	Unrelated / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0007	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	12FEB2020 (8)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19FEB2020 (15)	25FEB2020 (21)	Grade 3	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	19FEB2020 (15)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	26FEB2020 (22)	04MAR2020 (29)	Grade 4	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No
			Nervous system disorders / Parkinsonian rest tremor / WORSENER PARKINSON'S TREMOR IN LEFT HAND AND FOOT	26FEB2020 (22)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	26FEB2020 (22)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0007	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	28FEB2020 (24)	03MAR2020 (28)	Grade 2	Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / INTERMITTENT FATIGUE	04MAR2020 (29)	16JUN2020 (133)	Grade 1	Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	22APR2020 (78)	06MAY2020 (92)	Grade 1	Resolved	Medication	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17JUN2020 (134)		Grade 1	Not Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	17JUN2020 (134)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Corona virus infection / COVID-19	07NOV2020 (277)	24NOV2020 (294)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0007	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash pruritic / BILATERAL UPPER EXTREMITY AND LOWER EXTREMITY PRURITIC RASH	09DEC2020 (309)	10DEC2020 (310)	Grade 1	Resolved	Other: BENADRYL PREMEDIATION PRIOR TO INFUSIONS	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0108-0009	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / INTERMITTENT NAUSEA	11MAR2020 (8)		Grade 1	Not Resolved	Medication; Other: SWITCHED TO CARBOPLATIN	Unrelated / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	25MAR2020 (22)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01APR2020 (29)		Grade 1	Not Resolved	Other: SWITCHED TO CARBOPLATIN	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLI	22MAY2020 (80)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0108-0009	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	03JUN2020 (92)	10JUN2020 (99)	Grade 3	Resolved	Other: PRBC TRANSFUSION	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / INTERMITTENT LEFT CHEST PAIN (NON-CARDIAC)	12AUG2020 (162)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / DYSPNEA ON EXERTION	26AUG2020 (176)		Grade 2	Not Resolved	Other: 2L O2	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / LEFT-SIDED ABDOMINAL PAIN	21OCT2020 (232)		Grade 2	Not Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Missing / Missing / Missing	No
0110-0001	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Erythema / INTERMITTENT EPISODES OF FACIAL REDNESS	02AUG2018 (3)	20SEP2018 (52)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / INTERMITTENT NAUSEA	04AUG2018 (5)	19NOV2018 (112)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0110-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	22AUG2018 (23)	29AUG2018 (30)	Grade 3	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	22AUG2018 (23)	19NOV2018 (112)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	29AUG2018 (30)	19NOV2018 (112)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Hypoaesthesia / EPISODE OF RIGHT HAND AND FINGER NUMBNESS	11SEP2018 (43)	11SEP2018 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERY EYES	10OCT2018 (72)	19NOV2018 (112)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RHINORRHEA	10OCT2018 (72)	19NOV2018 (112)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0110-0002	ADIPemPlatinum	Yes	Nervous system disorders / Headache / EPISODE OF MILD HEADACHE	14FEB2019 (3)	14FEB2019 (3)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0110-0002	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTAXIS	18FEB2019 (7)	20FEB2019 (9)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	19FEB2019 (8)	20FEB2019 (9)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	21FEB2019 (10)		Grade 1	Not Resolved	Medication	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	21FEB2019 (10)		Grade 1	Not Resolved	None	Probably /	Dose Not Changed /	No
			Renal and urinary disorders / Urinary incontinence / EPISODE OF URINARY INCONTINENCE	24FEB2019 (13)	14MAR2019 (31)	Grade 1	Resolved	Medication	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	28FEB2019 (17)		Grade 1	Not Resolved	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	08MAR2019 (25)	27MAR2019 (44)	Grade 1	Resolved	Medication	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0110-0002	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / MILD RIGHT SHOULDER PAIN	08MAR2019 (25)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / INTERMITTENT NEUTROPENIA	09MAR2019 (26)	19APR2019 (67)	Grade 2	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / NASAL DRAINAGE	22MAR2019 (39)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	12APR2019 (60)	13APR2019 (61)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0112-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / WORSENING LEFT SIDE CHEST PAIN (NON CARDIAC) GR. 3	02SEP2019 (8)	03SEP2019 (9)	Grade 3	Resolved with Sequelae	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	02SEP2019 (8)		Grade 1	Unknown	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0112-0002	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	03SEP2019 (9)	03SEP2019 (9)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Oedema peripheral / WORSENING BILATERAL LOWER EXTREMITY EDEMA	10SEP2019 (16)		Grade 3	Unknown	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Decubitus ulcer / SKIN ULCERATION (SACRAL AREA_	10SEP2019 (16)		Grade 1	Unknown	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	13SEP2019 (19)	16SEP2019 (22)	Grade 3	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	16SEP2019 (22)		Grade 2	Not Resolved	Other: DISCONTINU ED	Unlikely / Probably / Not Applicable / Probably	Drug Withdrawn / Drug Withdrawn / Not Applicable / Drug Withdrawn	No
0112-0003	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Gastrooesophageal reflux disease / HEART BURN (GERD)	27SEP2019 (4)	03OCT2019 (10)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0112-0003	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / INTERMITTENT NAUSEA	27SEP2019 (4)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27SEP2019 (4)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	27SEP2019 (4)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Nasal congestion / INTERMITTENT NASAL CONGESTION	27SEP2019 (4)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	12OCT2019 (19)	15OCT2019 (22)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash / RASH - CHEST	26NOV2019 (64)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Toothache / TOOTH ACHE	07DEC2019 (75)	27DEC2019 (95)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0112-0003	PlaceboPemPlatinum	Yes	Infections and infestations / Tooth infection / TOOTH INFECTION	07DEC2019 (75)	27DEC2019 (95)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Abdominal pain upper / STOMACH PAIN	09DEC2019 (77)	13DEC2019 (81)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Dizziness / DIZZINESS - INTERMITTENT	19DEC2019 (87)	04FEB2020 (134)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	09JAN2020 (108)	14JAN2020 (113)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Vomiting / VOMITTING	09JAN2020 (108)	14JAN2020 (113)	Grade 1	Resolved	Medication	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	27JAN2020 (126)	04FEB2020 (134)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	27JAN2020 (126)	04FEB2020 (134)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0112-0003	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pain / PAIN RIGHT SIDE	28JAN2020 (127)	01FEB2020 (131)	Grade 1	Resolved with Sequelae	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Abdominal pain upper / RIGHT UPPER QUADRANT ABDOMINAL PAIN	02FEB2020 (132)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Rib fracture / 8TH RIB FRACTURE	27FEB2020 (157)	25MAR2020 (184)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0001	PlaceboPemPlatinum	Yes	Eye disorders / Dry eye / DRY EYES	01AUG2017 (-1)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / TASTE CHANGE	01AUG2017 (-1)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	06AUG2017 (5)	12SEP2017 (42)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	06AUG2017 (5)	12SEP2017 (42)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0001	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	06AUG2017 (5)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	23AUG2017 (22)	31OCT2017 (91)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	12SEP2017 (42)	12SEP2017 (42)	Grade 1	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12SEP2017 (42)	24OCT2017 (84)	Grade 2	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	12SEP2017 (42)	06DEC2017 (127)	Grade 2	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Myalgia / MYALGIA	12SEP2017 (42)		Grade 1	Ongoing	Medication	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	12SEP2017 (42)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0001	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Myalgia / MYALGIA	20SEP2017 (50)	22SEP2017 (52)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Pain in extremity / PAIN IN THE EXTREMITY	20SEP2017 (50)	22SEP2017 (52)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Myalgia / LEFT THIGH MYALGIA	02OCT2017 (62)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	03OCT2017 (63)	09OCT2017 (69)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye irritation / BURNING EYES	03OCT2017 (63)	25OCT2017 (85)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	24OCT2017 (84)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Lymphadenopathy / LYMPHADENOPATHY-GROIN SWELLING	25OCT2017 (85)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0001	PlaceboPemPlatinum	Yes	Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	05NOV2017 (96)	14NOV2017 (105)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST PAIN (NON-CARDIAC; CHEST INFECTION)	05NOV2017 (96)	14NOV2017 (105)	Grade 1	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	09NOV2017 (100)	30NOV2017 (121)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	15AUG2017 (7)	16AUG2017 (8)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Reduced / Drug Withdrawn / Not Applicable	Yes
			Nervous system disorders / Dizziness / LIGHT HEADED	03SEP2017 (26)		Grade 1	Ongoing	None	Unrelated / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	11SEP2017 (34)	18SEP2017 (41)	Grade 1	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Haemoglobin decreased / LOW HB LEVELS	12SEP2017 (35)	19SEP2017 (42)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unrelated / Definitely / Unrelated / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0002	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	28SEP2017 (51)		Grade 1	Ongoing	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	28SEP2017 (51)		Grade 1	Ongoing	Medication	Unrelated / Unlikely / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed; Dose Reduced	No
			Nervous system disorders / Dizziness / DIZZINESS	01OCT2017 (54)	03OCT2017 (56)	Grade 1	Resolved	Other: IV FLUIDS	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Sepsis / CHEST SEPSIS	08OCT2017 (61)	10OCT2017 (63)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Not Applicable / Unlikely	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0201-0004	PlaceboPemPlatinum	Yes	Nervous system disorders / Tremor / TREMOR	09SEP2017 (4)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	13SEP2017 (8)	17OCT2017 (42)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0004	PlaceboPemPlatinum	Yes	Injury, poisoning and procedural complications / Toxicity to various agents / OPIOID TOXICITY	15SEP2017 (10)	19SEP2017 (14)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization; Other: ADMITTED TO CHURCHILL HOSPITAL WITH DROWSINESS TO OPIOID TOXICITY.	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	Yes
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	04OCT2017 (29)		Grade 1	Ongoing	Other: BLOOD TRANSFUSIO N	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	15SEP2017 (3)	15OCT2017 (33)	Grade 2	Resolved	Other: DOSE CHANGED	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	17SEP2017 (5)	25SEP2017 (13)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17SEP2017 (5)	25SEP2017 (13)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0005	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Skin ulcer / SKIN ULCERATION	07OCT2017 (25)	08OCT2017 (26)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	07OCT2017 (25)	09OCT2017 (27)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Paraesthesia / TINGLING IN FINGERTIPS	12OCT2017 (30)		Grade 1	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Ageusia / LOSS OF TASTE TO FOOD	15OCT2017 (33)	30DEC2017 (109)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / METALLIC TASTE	15OCT2017 (33)	30DEC2017 (109)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Injection site reaction / INJECTION SITE REACTION	15OCT2017 (33)	02MAY2018 (232)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	16OCT2017 (34)	31OCT2017 (49)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pain / INCREASE PAIN - TOP RIGHT SHOULDER AND LOWER RIGHT RIB, BASE OF SPINE	16OCT2017 (34)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17OCT2017 (35)		Grade 2	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	17OCT2017 (35)		Grade 1	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	09NOV2017 (58)	06DEC2017 (85)	Grade 2	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	09NOV2017 (58)	06DEC2017 (85)	Grade 2	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	30NOV2017 (79)	09DEC2017 (88)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0005	ADIPemPlatinum	Yes	Eye disorders / Lacrimation increased / WATERING EYES	01DEC2017 (80)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	09JAN2018 (119)	18JAN2018 (128)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS	21FEB2018 (162)	25FEB2018 (166)	Grade 1	Resolved	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Urinary tract infection / URINE INFECTION	10APR2018 (210)	17APR2018 (217)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	15SEP2017 (3)	22SEP2017 (10)	Grade 2	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMIT	15SEP2017 (3)	22SEP2017 (10)	Grade 2	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	15SEP2017 (3)	22SEP2017 (10)	Grade 2	Resolved	Other: ADVICE GIVEN	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0006	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	17SEP2017 (5)	22SEP2017 (10)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	17SEP2017 (5)	22SEP2017 (10)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	23SEP2017 (11)	06NOV2017 (55)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	23SEP2017 (11)		Grade 1	Ongoing	Other: ADVICE GIVEN	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	01OCT2017 (19)	18NOV2017 (67)	Grade 1	Resolved	Other: TREATED WITH SUPPORTIVE ANTISICKNESS ONLY	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal distension / DISTENDED ABDOMEN	01OCT2017 (19)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0006	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	07OCT2017 (25)	18OCT2017 (36)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Cystitis / CYSTITIS	09OCT2017 (27)	16OCT2017 (34)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / MOUTH THRUSH	09OCT2017 (27)	18OCT2017 (36)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / MOUTH THRUSH	11OCT2017 (29)	19DEC2017 (98)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY BILATERAL EMBOLISM	18OCT2017 (36)	09FEB2018 (150)	Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / SHARP CHEST PAIN RADIATING TO BACK (NON-CARDIAC)	01NOV2017 (50)	01NOV2017 (50)	Grade 1	Resolved	Other: PATIENT ATTENDED LOCAL A&E, NO ADMISSION	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0006	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Pneumonitis / SUSPECTED PNEUMONITIS	30NOV2017 (79)	13DEC2017 (92)	Grade 2	Resolved	Medication	Unrelated / Possibly / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13DEC2017 (92)	02JAN2018 (112)	Grade 2	Ongoing	Other: ADVICE GIVEN	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02JAN2018 (112)		Grade 1	Ongoing	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	05JAN2018 (115)	06JAN2018 (116)	Grade 1	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	10JAN2018 (120)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Oral pain / SORE MOUTH	10JAN2018 (120)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY BILATERAL EMBOLISM	09FEB2018 (150)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Abdominal distension / BLOATED STOMACH	14OCT2017 (4)	24OCT2017 (14)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Dysgeusia / TASTE CHANGES	14OCT2017 (4)	05DEC2017 (56)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	15OCT2017 (5)	17OCT2017 (7)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	17OCT2017 (7)	20MAY2019 (587)	Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Not Applicable / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Palpitations / PALPITATIONS	05NOV2017 (26)	20MAY2019 (587)	Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	05NOV2017 (26)	20MAY2019 (587)	Grade 1	Resolving	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness / LIGHT HEADED	05NOV2017 (26)	20MAY2019 (587)	Grade 1	Ongoing	None	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA INTERMITTENT	13SEP2018 (51)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypertension / HYPERTENSION	05DEC2018 (134)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0009	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	28OCT2017 (4)	27DEC2017 (64)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	30OCT2017 (6)	27DEC2017 (64)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Dry eye / DRY EYES	08NOV2017 (15)	20NOV2017 (27)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Lip dry / DRY LIPS	08NOV2017 (15)		Grade 1	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Thirst / THIRSTY	08NOV2017 (15)		Grade 1	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0009	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Pleuritic pain / STABBING PAIN, DEEP INSIDE LUNG	27NOV2017 (34)	28NOV2017 (35)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02JAN2018 (70)	08JAN2018 (76)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Hypoaesthesia / NUMBNESS ON LEFT FOOT	09JAN2018 (77)		Grade 1	Ongoing	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	21JAN2018 (89)	21FEB2018 (120)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	24JAN2018 (92)	25JAN2018 (93)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / THRUSH ON TONGUE	24JAN2018 (92)	28JAN2018 (96)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0009	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Injection site bruising / BRUISE ON SITE OF INJECTION RIGHT ARM	25JAN2018 (93)	08FEB2018 (107)	Grade 1	Resolved	None	Definitely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	11FEB2018 (110)	15FEB2018 (114)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Muscle spasms / CRAMP-LEFT LEG	12FEB2018 (111)	13FEB2018 (112)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH OF FACE	17FEB2018 (116)	21FEB2018 (120)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	21FEB2018 (120)	21FEB2018 (120)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	05MAR2018 (132)		Grade 1	Ongoing	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	24MAR2018 (151)	01APR2018 (159)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0009	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	24MAR2018 (151)	04APR2018 (162)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	28MAR2018 (155)	04APR2018 (162)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Weight increased / WEIGHT INCREASE BY 10%	18MAY2018 (206)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / KNEE PAIN	30MAY2018 (218)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Sunburn / SUNBURN SENSATION OF THE SKIN	09JUN2018 (228)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / RIGHT CRAMP PAIN-BACK	04AUG2018 (284)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0009	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NOT CARDIAC-INTENSE PAIN IN STERNUM (AT NIGHT)	22SEP2018 (333)		Grade 1	Ongoing	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Hypoaesthesia / NUMBNESS UNDER RIGHT ARM AND SIDE OF RIGHT BUST.	24SEP2018 (335)		Grade 1	Ongoing	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON FACE	27NOV2018 (399)		Grade 1	Ongoing	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain lower / PAIN ON RIGHT SIDE- NEAR PELVIS	29NOV2018 (401)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Hyperhidrosis / SWEATING ON FOREHEAD	29NOV2018 (401)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Flank pain / INCREASING ABDOMINAL PAIN IN RIGHT FLANK	06JAN2019 (439)	08JAN2019 (441)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0011	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	27JAN2018 (46)	27MAR2018 (105)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	24MAR2018 (102)	31MAR2018 (109)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	30MAR2018 (108)	30APR2018 (139)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	18APR2018 (127)		Grade 2	Resolving	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0013	ADIPemPlatinum	Yes	Nervous system disorders / Neuropathy peripheral / NEUROPATHY	05FEB2018 (6)	02MAR2018 (31)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA INTERMITTENT	05FEB2018 (6)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE INTERMITTENT	09FEB2018 (10)		Grade 1	Resolving	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0013	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Epistaxis / NOSE BLEED	13FEB2018 (14)	13FEB2018 (14)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS INTERMITTENT	15FEB2018 (16)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	25FEB2018 (26)		Grade 1	Resolving	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	28FEB2018 (29)	06MAR2018 (35)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye pain / SORE EYES INTERMITTENT	08MAR2018 (37)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Chills / SHIVERS INTERMITTENT	17MAR2018 (46)	21MAR2018 (50)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Cystitis / CYSTITIS	28MAR2018 (57)	04APR2018 (64)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0013	ADIPemPlatinum	Yes	Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	26APR2018 (86)	24JUN2018 (145)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	15MAY2018 (105)	28MAY2018 (118)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Hypoacusis / REDUCED HEARING	17MAY2018 (107)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	17MAY2018 (107)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0014	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	18FEB2018 (5)	05APR2018 (51)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	18FEB2018 (5)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	01MAR2018 (16)	08MAR2018 (23)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0014	PlaceboPemPlatinum	Yes	Nervous system disorders / Dysgeusia / TASTE CHANGE	01MAR2018 (16)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	11MAR2018 (26)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Myopathy / PROXIMAL MYOPATHY	11MAR2018 (26)		Grade 2	Ongoing	Other: REDUCED DEXAMETHASONE TO 2MG	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	22MAR2018 (37)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	27MAR2018 (42)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / BILATERAL CENTRAL PULMONARY EMBOLISM	02APR2018 (48)	05APR2018 (51)	Grade 4	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Infections and infestations / Genital infection fungal / FUNGAL INFECTION-PENIS	08APR2018 (54)	21APR2018 (67)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0014	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Decubitus ulcer / PRESSURE SORE	10APR2018 (56)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	10APR2018 (56)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Peripheral swelling / SWOLLEN LEGS	13APR2018 (59)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / PAIN - RIGHT LOWER BACK	14APR2018 (60)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0015	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA INTERMITTENT	18MAR2018 (5)	12JUL2018 (121)	Grade 1	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE INTERMITTENT	18MAR2018 (5)		Grade 1	Resolving	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	20MAR2018 (7)	20MAR2018 (7)	Grade 1	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0015	ADIPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	20MAR2018 (7)	21MAR2018 (8)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	21MAR2018 (8)	21MAR2018 (8)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	03APR2018 (21)	09APR2018 (27)	Grade 3	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Eye disorders / Vision blurred / BLURRED VISION	05APR2018 (23)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			INTERMITTENT Respiratory, thoracic and mediastinal disorders / Cough / MILD COUGH	16APR2018 (34)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Immune system disorders / Hypersensitivity / ALLERGIC REACTION	18APR2018 (36)	25APR2018 (43)	Grade 2	Resolved	Medication	Definitely / Unrelated / Unrelated / Not Applicable	Drug Interrupted; Drug Withdrawn / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Skin and subcutaneous tissue disorders / Rash / RASH RIGHT ARM	18APR2018 (36)	26APR2018 (44)	Grade 2	Resolved	Medication	Probably / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0016	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	09APR2018 (6)	04JUN2018 (62)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	10APR2018 (7)	17APR2018 (14)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	26APR2018 (23)	11SEP2018 (161)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / INTERMITTENT FATIGUE	26APR2018 (23)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	27APR2018 (24)	01MAY2018 (28)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY FINGERS/LEFT FEET	27APR2018 (24)	16JUL2018 (104)	Grade 1	Resolved	None	Unrelated / Probably / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	02MAY2018 (29)	22MAY2018 (49)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0016	PlaceboPemPlatinum	Yes	Vascular disorders / Arteriosclerosis / ATHEROSCLEROSIS	14MAY2018 (41)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH INTERMITTENT	16MAY2018 (43)	22MAY2018 (49)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Sputum abnormal / SPUTUM CHANGES	22MAY2018 (49)	04JUL2018 (92)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH - RELATED TO DISEASE (CANCER)	22MAY2018 (49)	04JUL2018 (92)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Procedural vomiting / VOMITING- TREATMENT RELATED	04JUN2018 (62)	10JUL2018 (98)	Grade 2	Resolved	Medication	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	04JUN2018 (62)	10JUL2018 (98)	Grade 2	Resolved	None	Unrelated / Possibly / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0016	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hyperuricaemia / HYPERURICEMIA	11JUN2018 (69)	15JUN2018 (73)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization; Other: MEDICATION	Possibly / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE RENAL FAILURE	11JUN2018 (69)	26JUN2018 (84)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	11JUN2018 (69)	04JUL2018 (92)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	21JUN2018 (79)	27JUN2018 (85)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	04JUL2018 (92)	07JUL2018 (95)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / CLEAR PHLEGM	04JUL2018 (92)	07JUL2018 (95)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Post-tussive vomiting / VOMITING - RELATED TO COUGH	04JUL2018 (92)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0016	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	04JUL2018 (92)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	11JUL2018 (99)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC RIGHT CHEST PAIN	07AUG2018 (126)		Grade 1	Resolving	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	09OCT2018 (189)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13NOV2018 (224)	16NOV2018 (227)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / CHEST PAIN (NON-CARDIAC)	25MAR2019 (356)	26MAR2019 (357)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0017	PlaceboPemPlatinum	Yes	Nervous system disorders / Dysgeusia / TASTE CHANGE	01MAY2018 (7)	14AUG2018 (112)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Lip pain / SORE LIPS	05MAY2018 (11)	14AUG2018 (112)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	04JUN2018 (41)	11JUN2018 (48)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	19JUN2018 (56)	21JUN2018 (58)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Nervous system disorders / Lethargy / LETHARGY	03JUL2018 (70)		Grade 2	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Skin and subcutaneous tissue disorders / Decubitus ulcer / BED SORES	03JUL2018 (70)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	18JUL2018 (85)	19JUL2018 (86)	Grade 1	Resolved	Other: BLOOD TRANSFUSION	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Withdrawn / Drug Withdrawn / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0017	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / ANKLE OEDEMA	28JUL2018 (95)		Grade 2	Ongoing	Medication	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain upper / RIGHT SUB DIAPHRAGMATIC PAIN	31JUL2018 (98)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Staphylococcal infection / MRSA POSITIVE	31JUL2018 (98)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Localised infection / LEFT HEEL INFECTION	07AUG2018 (105)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0018	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / BACK RASH	01MAY2018 (1)	01MAY2018 (1)	Grade 1	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	03MAY2018 (3)	03MAY2018 (3)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA - INTERMITTENT	04MAY2018 (4)	18AUG2018 (110)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0018	ADIPemPlatinum	Yes	General disorders and administration site conditions / Chest discomfort / CHEST TIGHTNESS	08MAY2018 (8)	08MAY2018 (8)	Grade 1	Resolved	Medication	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Blister / BLISTERS - NECK	08MAY2018 (8)	10MAY2018 (10)	Grade 1	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / TASTE CHANGE	08MAY2018 (8)	28AUG2018 (120)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Immune system disorders / Hypersensitivity / ALLERGY	16MAY2018 (16)	18MAY2018 (18)	Grade 2	Resolved	Medication	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	10JUL2018 (71)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	10JUL2018 (71)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	17JUL2018 (78)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0018	ADIPemPlatinum	Yes	Ear and labyrinth disorders / Deafness / HEARING LOSS	01NOV2018 (185)	22DEC2018 (236)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY- RIGHT HAND	08NOV2018 (192)	01MAY2019 (366)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LOWER RIGHT BACK PAIN	07JAN2019 (252)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Unknown / Unknown / Unknown	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / RIGHT SIDE SHOULDER PAIN	07JAN2019 (252)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Unknown / Unknown / Unknown	No
			Psychiatric disorders / Insomnia / INSOMNIA	01MAR2019 (305)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0019	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA INTERMITTENT	12MAY2018 (4)	11SEP2018 (126)	Grade 1	Resolved	None	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0019	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE INTERMITTENT	13MAY2018 (5)	16JUL2018 (69)	Grade 1	Resolved	None	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY INTERMITTENT	17MAY2018 (9)		Grade 1	Resolving	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	30MAY2018 (22)	13JUN2018 (36)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Investigations / Blood creatinine increased / INCREASED CREATININE	04JUN2018 (27)	15JUN2018 (38)	Grade 1	Resolved	Other: CISPLATIN REDUCED BY 50%	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Nasal congestion / NASAL CONGESTION	16JUL2018 (69)	18JUL2018 (71)	Grade 1	Resolved	Medication	Unrelated / Possibly / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood creatinine increased / INCREASED CREATININE	16JUL2018 (69)	25JUL2018 (78)	Grade 1	Resolved	Other: CISPLATIN WITHDRAWN	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	16JUL2018 (69)	10SEP2018 (125)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0019	ADIPemPlatinum	Yes	Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	23JUL2018 (76)	30JUL2018 (83)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	01AUG2018 (85)	19SEP2018 (134)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	06AUG2018 (90)	14AUG2018 (98)	Grade 3	Resolved	None	Unrelated / Possibly / Not Applicable / Definitely	Dose Not Changed / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	09SEP2018 (124)	11SEP2018 (126)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0201-0020	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	13JUN2018 (8)	10OCT2018 (127)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	13JUN2018 (8)	10OCT2018 (127)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	26JUN2018 (21)	28AUG2018 (84)	Grade 1	Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0020	PlaceboPemPlatinum	Yes	Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	22AUG2018 (78)	25AUG2018 (81)	Grade 1	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0021	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	21JUL2018 (25)	01AUG2018 (36)	Grade 2	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	21JUL2018 (25)	01AUG2018 (36)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / APPETITE LOSS	08AUG2018 (43)	30AUG2018 (65)	Grade 2	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Angina pectoris / LEFT SIDE CARDIAC CHEST PAIN	16OCT2018 (112)	29DEC2018 (186)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	17OCT2018 (113)		Grade 2	Ongoing	Medication	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Psychiatric disorders / Anxiety / ANXIETY	18OCT2018 (114)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0022	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	08JUL2018 (5)		Grade 3	Ongoing	None	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	08JUL2018 (5)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Fluid intake reduced / LOW FLUID INTAKE	08JUL2018 (5)		Grade 3	Ongoing	Other: FLUIDS GIVEN	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0023	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH EACH HAND	01AUG2018 (15)	08AUG2018 (22)	Grade 1	Resolved	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH LOWER LIMBS	03AUG2018 (17)	04AUG2018 (18)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	06AUG2018 (20)	18SEP2018 (63)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	12SEP2018 (57)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0023	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	13SEP2018 (58)	11DEC2018 (147)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	26SEP2018 (71)	04OCT2018 (79)	Grade 2	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	05OCT2018 (80)	09OCT2018 (84)	Grade 3	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	11OCT2018 (86)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11OCT2018 (86)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29OCT2018 (104)	07NOV2018 (113)	Grade 2	Resolved	Medication	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	14NOV2018 (120)	28NOV2018 (134)	Grade 2	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0023	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	12DEC2018 (148)	19DEC2018 (155)	Grade 2	Resolved	Medication	Unrelated / Probably / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	16FEB2019 (214)	25FEB2019 (223)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / COUGH (CLEAR PHLEGM)	27MAR2019 (253)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0024	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA INTERMITTENT	06AUG2018 (6)	22AUG2018 (22)	Grade 1	Resolved	Medication	Possibly / Possibly / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	06AUG2018 (6)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE INTERMITTENT	06AUG2018 (6)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	15AUG2018 (15)	19DEC2018 (141)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0024	ADIPemPlatinum	Yes	Investigations / Blood creatinine increased / INCREASED CREATININE	22AUG2018 (22)		Grade 1	Ongoing	Other: CISPLATIN REDUCED	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Anorectal discomfort / SORE ANNUS	28AUG2018 (28)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH UPPER ARMS	05SEP2018 (36)		Grade 1	Ongoing	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	07SEP2018 (38)	10OCT2018 (71)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / TASTE CHANGES	20SEP2018 (51)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	06JAN2019 (159)		Grade 3	Ongoing	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes
			Infections and infestations / Pneumonia / PNEUMONIA	06JAN2019 (159)		Grade 3	Ongoing	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0025	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain lower / LEFT LOWER QUADRANT PAIN	18NOV2018 (5)	22NOV2018 (9)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	04JAN2019 (52)	16JAN2019 (64)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	04JAN2019 (52)	09APR2019 (147)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	04JAN2019 (52)		Grade 1	Ongoing	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	04JAN2019 (52)		Grade 1	Ongoing	None	Possibly / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	08JAN2019 (56)	09JAN2019 (57)	Grade 1	Resolved with Sequelae	None	Unrelated / Probably / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY FAILURE	15JAN2019 (63)	17JAN2019 (65)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Withdrawn / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0025	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	06MAR2019 (113)	09APR2019 (147)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	01JUN2019 (200)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0026	PlaceboPemPlatinum	Yes	Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	12SEP2018 (8)	19SEP2018 (15)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	25SEP2018 (21)	27SEP2018 (23)	Grade 2	Resolved	Medication	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	25SEP2018 (21)	27SEP2018 (23)	Grade 2	Resolved	Medication	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Alopecia / HAIR LOSS	25SEP2018 (21)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	03OCT2018 (29)	11OCT2018 (37)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0026	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	03OCT2018 (29)	11OCT2018 (37)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
0201-0027	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Fluid intake reduced / REDUCED FLUID INTAKE	05OCT2018 (4)	14OCT2018 (13)	Grade 2	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / INTERMITTENT NAUSEA	05OCT2018 (4)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	05OCT2018 (4)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LOWER BACK PAIN	05OCT2018 (4)		Grade 2	Ongoing	Medication	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / RIGHT PLEURAL PAIN	05OCT2018 (4)		Grade 2	Ongoing	Medication	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	06OCT2018 (5)	14OCT2018 (13)	Grade 3	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0027	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	08OCT2018 (7)	11OCT2018 (10)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	09OCT2018 (8)	11OCT2018 (10)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	09OCT2018 (8)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	25OCT2018 (24)	01NOV2018 (31)	Grade 2	Resolved	Medication	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / REDUCED NEUTROPHIL COUNT	30OCT2018 (29)	06NOV2018 (36)	Grade 4	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	30OCT2018 (29)	06NOV2018 (36)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Withdrawn / Not Applicable	Yes
			Gastrointestinal disorders / Vomiting / VOMITING	18NOV2018 (48)	20NOV2018 (50)	Grade 1	Resolved	None	Unrelated / Definitely / Unrelated / Not Applicable	Unknown / Unknown / Unknown / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0027	PlaceboPemPlatinum	Yes	Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	04DEC2018 (64)	08DEC2018 (68)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Unlikely / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	17DEC2018 (77)	25JAN2019 (116)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Not Applicable / Not Applicable	Yes
0201-0028	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Gastroesophageal reflux disease / ACID REFLUX	24OCT2018 (8)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	11NOV2018 (26)	14NOV2018 (29)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	11NOV2018 (26)	28NOV2018 (43)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Orthostatic hypotension / POSTURAL HYPOTENSION	14NOV2018 (29)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	18DEC2018 (63)	25DEC2018 (70)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0028	PlaceboPemPlatinum	Yes	Nervous system disorders / Dizziness / DIZZINESS	18DEC2018 (63)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0030	PlaceboPemPlatinum	Yes	Ear and labyrinth disorders / Deafness / HEARING LOSS	24OCT2018 (8)	29JAN2019 (105)	Grade 2	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Dose Not Changed	No
			Ear and labyrinth disorders / Deafness / HEARING LOSS	29JAN2019 (105)		Grade 3	Not Resolved	Other: CISPLATIN NOT GIVEN	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Investigations / Haemoglobin decreased / LOW HAEMOGLOBIN	06FEB2019 (113)	09FEB2019 (116)	Grade 1	Resolved	Other: BLOOD TRANSFUSION	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0031	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	11NOV2018 (12)	06DEC2018 (37)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	19NOV2018 (20)	27NOV2018 (28)	Grade 1	Resolved	Other: TREATMENT DELAYED.	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0031	ADIPemPlatinum	Yes	General disorders and administration site conditions / Injection site rash / RASH AROUND INJECTION SITE ON BOTH ARMS	07DEC2018 (38)	22DEC2018 (53)	Grade 1	Resolved	None	Definitely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	20DEC2018 (51)	20JAN2019 (82)	Grade 1	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Gastric pH decreased / INCREASED GASTRIC ACID	03JAN2019 (65)	01FEB2019 (94)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH	29JAN2019 (91)		Grade 1	Ongoing	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Syncope / FAINT EPISODE	10SEP2019 (315)	10SEP2019 (315)	Grade 3	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	10JAN2020 (437)	28JAN2020 (455)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	18FEB2020 (476)	27FEB2020 (485)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0033	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	23JAN2019 (8)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH	04FEB2019 (20)	18MAR2019 (62)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / LEFT CHEST WALL PAIN	04MAR2019 (48)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Diabetes mellitus / STEROID INDUCED DIABETES	08APR2019 (83)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH	15APR2019 (90)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	01MAY2019 (106)		Grade 1	Ongoing	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
0201-0034	ADIPemPlatinum	Yes	Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	13DEC2018 (9)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0034	ADIPemPlatinum	Yes	Investigations / Blood creatinine increased / CREATININE INCREASED	24JAN2019 (51)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHIL	20FEB2019 (78)	28MAY2019 (175)	Grade 2	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHIL	27FEB2019 (85)	06MAR2019 (92)	Grade 3	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHIL	06MAR2019 (92)	11MAR2019 (97)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHIL	28MAR2019 (114)	11APR2019 (128)	Grade 3	Resolved with Sequelae	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	25APR2019 (142)	09MAY2019 (156)	Grade 1	Resolved	None	Unlikely / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	12SEP2019 (282)	19SEP2019 (289)	Grade 2	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0035	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	12DEC2018 (8)	24DEC2018 (20)	Grade 1	Resolved with Sequelae	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Insomnia / INSOMNIA	12DEC2018 (8)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23JAN2019 (50)	13FEB2019 (71)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13FEB2019 (71)	19FEB2019 (77)	Grade 3	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13FEB2019 (71)		Grade 1	Ongoing	Medication	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	18FEB2019 (76)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20FEB2019 (78)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0035	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Diabetes mellitus / DIABETES	27FEB2019 (85)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	20MAR2019 (106)		Grade 1	Ongoing	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	20APR2019 (137)	24APR2019 (141)	Grade 1	Resolved with Sequelae	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Drug Withdrawn / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	15MAY2019 (162)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0036	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	08DEC2018 (4)		Grade 2	Ongoing	None	Unlikely / Probably / Probably / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	12DEC2018 (8)		Grade 1	Ongoing	None	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	12DEC2018 (8)		Grade 2	Ongoing	Medication	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0036	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	08JAN2019 (35)		Grade 3	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0038	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	30JAN2019 (15)		Grade 1	Ongoing	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / SORE MOUTH (MUCOSITIS)	01FEB2019 (17)	30MAY2019 (135)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHILS	06FEB2019 (22)	12FEB2019 (28)	Grade 3	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / FEET NEUROPATHY	10FEB2019 (26)		Grade 1	Not Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	12FEB2019 (28)	19FEB2019 (35)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Influenza like illness / FLU-LIKE SYMPTOMS	01MAY2019 (106)	08MAY2019 (113)	Grade 1	Resolved with Sequelae	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0038	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANAEMIA	07MAY2019 (112)	17MAY2019 (122)	Grade 2	Resolved with Sequelae	Other: BLOOD TRANSFUSION	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	11JUN2019 (147)	06AUG2019 (203)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Chest discomfort / RIGHT SIDE CHEST TIGHTNESS	06AUG2019 (203)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0039	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION	30JAN2019 (1)	30JAN2019 (1)	Grade 3	Resolved with Sequelae	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHILS	20FEB2019 (22)	28FEB2019 (30)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Unknown	No
			Gastrointestinal disorders / Abdominal distension / BLOATEDNESS	21FEB2019 (23)	30MAY2019 (121)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0039	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	21FEB2019 (23)	30MAY2019 (121)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / SKIN RASH	21FEB2019 (23)	30MAY2019 (121)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Angina pectoris / CARDIAC CHEST PAIN	23FEB2019 (25)	25FEB2019 (27)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	11APR2019 (72)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
0201-0040	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RUNNY NOSE	10FEB2019 (-2)	30JUN2019 (139)	Grade 1	Resolved	None	Unrelated / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	12FEB2019 (1)	01MAR2019 (18)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / LOOSE STOOLS	19FEB2019 (8)	26FEB2019 (15)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0040	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / LUMP IN THROAT SENSATION - MUCOSITIS	19FEB2019 (8)	25JUN2019 (134)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Ear and labyrinth disorders / Deafness / HEARING LOSS	19FEB2019 (8)	15JUL2019 (154)	Grade 1	Resolved	Other: CISPLATIN WITHDRAWN , SWITCHED TO CARBO	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	01MAR2019 (18)	30JUN2019 (139)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / TASTE CHANGES	01MAR2019 (18)	30JUN2019 (139)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal distension / ABDO DISTENDED	02APR2019 (50)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	17APR2019 (65)	18JUN2019 (127)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0040	PlaceboPemPlatinum	Yes	Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	14MAY2019 (92)	16MAY2019 (94)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	04SEP2019 (205)	12SEP2019 (213)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	11DEC2019 (303)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Dyspepsia / HEARTBURN	23DEC2019 (315)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	06JAN2020 (329)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Infections and infestations / Corona virus infection / COVID-19	20MAR2020 (403)	27MAR2020 (410)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Infections and infestations / Pneumonia / PNEUMONIA	20MAR2020 (403)	27MAR2020 (410)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0041	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	03APR2019 (1)	31JUL2019 (120)	Grade 1	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	03APR2019 (1)	31JUL2019 (120)	Grade 1	Resolved	Medication	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	03APR2019 (1)	31JUL2019 (120)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Immune system disorders / Seasonal allergy / HAYFEVER	12MAY2019 (40)	04SEP2019 (155)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHILS	13MAY2019 (41)	20MAY2019 (48)	Grade 3	Resolved with Sequelae	None	Unlikely / Possibly / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	05JUN2019 (64)	12JUN2019 (71)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHILS	19JUN2019 (78)	26JUN2019 (85)	Grade 4	Resolved with Sequelae	None	Unlikely / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0041	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Pruritus / ITCHING AROUND UPPER ARM AREA	21JUN2019 (80)		Grade 1	Ongoing	None	Probably / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHILS	26JUN2019 (85)	24JUL2019 (113)	Grade 3	Resolved	None	Unlikely / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / ARM RASH	02JUL2019 (91)		Grade 1	Ongoing	Medication	Probably / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Skin abrasion / ABRASION TO KNEE	19AUG2019 (139)	04SEP2019 (155)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	Yes
			Nervous system disorders / Paraesthesia / PARATHESIA	16OCT2019 (197)		Grade 1	Resolving	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0043	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / BILATERAL UPPER ARM RASH	28MAY2019 (21)		Grade 1	Ongoing	None	Definitely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0043	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	25AUG2019 (110)	04SEP2019 (120)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	04SEP2019 (120)		Grade 1	Ongoing	None	Unlikely / Probably / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	23OCT2019 (169)		Grade 2	Ongoing	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	23OCT2019 (169)		Grade 1	Ongoing	None	Unlikely / Possibly / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0044	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	22MAY2019 (8)		Grade 1	Ongoing	Medication	Unlikely / Probably / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Tremor / HAND TREMOR	01JUN2019 (18)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	03JUL2019 (50)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0044	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Bone pain / BONE PAIN	19SEP2019 (128)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	04NOV2019 (174)	23DEC2019 (223)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	06NOV2019 (176)	08JAN2020 (239)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Chills / CHILLS	13JAN2020 (244)	13JAN2020 (244)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Bone pain / BONE PAIN	27MAR2020 (318)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0045	PlaceboPemPlatinum	Yes	Ear and labyrinth disorders / Tinnitus / TINNITUS	29APR2019 (6)	03JUN2019 (41)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13MAY2019 (20)	21AUG2019 (120)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0045	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	22MAY2019 (29)	29MAY2019 (36)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	25MAY2019 (32)	21AUG2019 (120)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	25MAY2019 (32)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Tooth abscess / TOOTH ABSCESS	08JUL2019 (76)	31JUL2019 (99)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / KNEE PAIN	23OCT2019 (183)	05NOV2019 (196)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Colitis / COLITIS	29OCT2019 (189)	05NOV2019 (196)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Tendon pain / ACHILLES PAIN	08JAN2020 (260)	29JAN2020 (281)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0045	PlaceboPemPlatinum	Yes	Infections and infestations / Tooth infection / TOOTH INFECTION	27FEB2020 (310)	05MAR2020 (317)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	11JUN2020 (415)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0046	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	17MAY2019 (3)	22MAY2019 (8)	Grade 2	Resolved with Sequelae	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	18JUL2019 (65)		Grade 1	Ongoing	Medication	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	18JUL2019 (65)		Grade 1	Ongoing	None	Unlikely / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31JUL2019 (78)		Grade 1	Ongoing	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	04SEP2019 (113)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0047	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	18MAY2019 (4)	03JUN2019 (20)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	05JUN2019 (22)	07JUN2019 (24)	Grade 1	Resolved with Sequelae	Medication	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	08JUN2019 (25)	09JUN2019 (26)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	Yes
			Gastrointestinal disorders / Vomiting / VOMITING	08JUN2019 (25)	09JUN2019 (26)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	10JUN2019 (27)		Grade 1	Ongoing	Medication	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain upper / UPPER LEFT QUADRANT PAIN	03JUL2019 (50)	17JUL2019 (64)	Grade 3	Resolved with Sequelae	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	03JUL2019 (50)		Grade 1	Ongoing	None	Unrelated / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0047	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / LEFT SIDE NON- CARDIAC CHEST PAIN	11AUG2019 (89)	16AUG2019 (94)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0201-0048	PlaceboPemPlatinum	Yes	Nervous system disorders / Dizziness / DIZZINESS	01JUN2019 (-3)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	07JUN2019 (4)		Grade 2	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	13JUN2019 (10)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	20JUN2019 (17)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	03JUL2019 (30)	12JUL2019 (39)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0048	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Pancytopenia / PANCYTOPENIC	04JUL2019 (31)	12JUL2019 (39)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Gouty tophus / GOUT WITH CRYSTALS	18JUL2019 (45)	29JUL2019 (56)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Probably / Probably / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0201-0049	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	04JUL2019 (10)		Grade 1	Ongoing	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	23JUL2019 (29)		Grade 2	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	25JUL2019 (31)	07AUG2019 (44)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Probably / Probably / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0201-0050	PlaceboPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	01AUG2019 (10)	01OCT2019 (71)	Grade 1	Resolved with Sequelae	None	Unrelated / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0050	PlaceboPemPlatinum	Yes	Eye disorders / Blepharitis / BLEPHARITIS	14AUG2019 (23)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	24OCT2019 (94)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14NOV2019 (115)	27NOV2019 (128)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0051	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / SHOULDER PAIN	07JUL2019 (6)		Grade 1	Ongoing	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	23JUL2019 (22)	20AUG2019 (50)	Grade 1	Resolved	Medication	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	02SEP2019 (63)	09SEP2019 (70)	Grade 2	Resolved with Sequelae	None	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0051	PlaceboPemPlatinum	Yes	Infections and infestations / Influenza / FLU	22OCT2019 (113)	29OCT2019 (120)	Grade 1	Resolved	Other: CHEMO DELAYED BY ONE WEEK	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	06NOV2019 (128)	19NOV2019 (141)	Grade 2	Resolved	Medication	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	26NOV2019 (148)		Grade 1	Ongoing	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	26NOV2019 (148)		Grade 1	Ongoing	None	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / JOINT PAIN	26NOV2019 (148)		Grade 1	Ongoing	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0201-0052	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	19JUL2019 (3)		Grade 1	Ongoing	None	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0052	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	19JUL2019 (3)		Grade 1	Ongoing	None	Possibly / Probably / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Infusion site bruising / BRUISING/DISCOLOURATION (AROUND INFUSION SITE)	31JUL2019 (15)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	06AUG2019 (21)	14AUG2019 (29)	Grade 2	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC LEFT CHEST PAIN	04SEP2019 (50)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	11SEP2019 (57)	16SEP2019 (62)	Grade 3	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	02OCT2019 (78)	07OCT2019 (83)	Grade 3	Resolved with Sequelae	Other: BLOOD TRANSFUSION N	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0052	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	02OCT2019 (78)	07OCT2019 (83)	Grade 2	Resolved with Sequelae	None	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0201-0053	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	22JUL2019 (6)	23JUL2019 (7)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	24JUL2019 (8)	28AUG2019 (43)	Grade 1	Not Resolved	Other: BLOOD TRANSFUSION	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	06AUG2019 (21)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	07AUG2019 (22)	12AUG2019 (27)	Grade 1	Resolved	Medication	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Reduced; Drug Interrupted / Not Applicable / Dose Reduced	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	28AUG2019 (43)	03SEP2019 (49)	Grade 2	Ongoing	Other: BLOOD TRANSFUSION	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0053	ADIPemPlatinum	Yes	Investigations / Neutrophil count decreased / LOW NEUTROPHIL	28AUG2019 (43)	03SEP2019 (49)	Grade 2	Ongoing	Medication	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	03SEP2019 (49)	10SEP2019 (56)	Grade 4	Resolved	None	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Investigations / White blood cell count decreased / LOW WHITE BLOOD CELLS	03SEP2019 (49)	10SEP2019 (56)	Grade 4	Resolved	None	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	03SEP2019 (49)	06NOV2019 (113)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23OCT2019 (99)	21NOV2019 (128)	Grade 1	Resolved	None	Possibly / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Reduced	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIC	06NOV2019 (113)	12NOV2019 (119)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Possibly / Possibly / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Reduced	No
			Investigations / Platelet count decreased / LOW PLATELETS	06NOV2019 (113)	12NOV2019 (119)	Grade 3	Resolved	Other: BLOOD TRANSFUSION	Possibly / Probably / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Reduced	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0053	ADIPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	06NOV2019 (113)		Grade 1	Ongoing	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	27NOV2019 (134)	12FEB2020 (211)	Grade 1	Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Platelet count decreased / LOW PLATELETS	27NOV2019 (134)	12FEB2020 (211)	Grade 2	Resolved with Sequelae	None	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Skin fissures / DRY/ CRACKED SKIN ON FINGERS	22JAN2020 (190)		Grade 1	Ongoing	Medication	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Cellulitis / CELLULTIS	04JUN2020 (324)	17JUN2020 (337)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	17JUN2020 (337)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0054	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Melaena / MELENA	24AUG2019 (4)	26AUG2019 (6)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	24AUG2019 (4)	05SEP2019 (16)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Possibly / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	26AUG2019 (6)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	06OCT2019 (47)	27NOV2019 (99)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	13NOV2019 (85)	04DEC2019 (106)	Grade 2	Resolved	Medication	Possibly / Probably / Not Applicable / Not Applicable	Drug Interrupted / Dose Not Changed / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Influenza like illness / FLU LIKE SYMPTOMS	10MAR2020 (203)	18MAR2020 (211)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	18MAR2020 (211)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0054	PlaceboPemPlatinum	Yes	Infections and infestations / Pneumonia / PNEUMONIA	28MAY2020 (282)	10JUN2020 (295)	Grade 3	Resolved with Sequelae	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	28MAY2020 (282)		Grade 3	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
0201-0057	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	15FEB2020 (6)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0201-0058	ADIPemPlatinum	Yes	Gastrointestinal disorders / Stomatitis / ORAL MUCOSITIS	18MAR2020 (23)	30MAR2020 (35)	Grade 2	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Empyema / EMPYEMA	24MAR2020 (29)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted; Drug Withdrawn / Drug Interrupted; Drug Withdrawn / Drug Interrupted; Drug Withdrawn / Not Applicable	Yes
			Nervous system disorders / Lethargy / EXTREME LETHARGY	24MAR2020 (29)		Grade 3	Ongoing	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0058	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	26MAR2020 (31)	28MAR2020 (33)	Grade 3	Resolved with Sequelae	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	29MAR2020 (34)		Grade 2	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0201-0060	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Muscular weakness / FALL DUE TO LOWER LIMB WEAKNESS	05MAY2021 (8)	19MAY2021 (22)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	06MAY2021 (9)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Definitely	Dose Not Changed / Dose Reduced / Not Applicable / Drug Interrupted	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	13MAY2021 (16)	18MAY2021 (21)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Fall / MECHANICAL FALL	26MAY2021 (29)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Reduced / Not Applicable / Drug Interrupted	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0201-0060	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Pancytopenia / PANCYTOPENIA	20JUN2021 (54)	09JUL2021 (73)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	Yes
			Infections and infestations / Sepsis / SEPSIS	20JUN2021 (54)	09JUL2021 (73)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	Yes
0201-0061	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	04JUL2021 (5)	21JUL2021 (22)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable / Dose Reduced; Drug Interrupted	No
			Infections and infestations / Pneumonia / BRONCHOPNEUMONIA	20SEP2021 (83)	21SEP2021 (84)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Not Applicable / Probably	Not Applicable / Not Applicable / Not Applicable	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	20SEP2021 (83)		Grade 4	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Gastritis / GASTRITIS	09APR2018 (6)	13APR2018 (10)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	09APR2018 (6)	13APR2018 (10)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCAEMIA	09APR2018 (6)	13APR2018 (10)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Nervous system disorders / Lethargy / LETHARGY	09APR2018 (6)	13APR2018 (10)	Grade 2	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Drug Interrupted / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	25APR2018 (22)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	28APR2018 (25)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0001	PlaceboPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	29APR2018 (26)	09MAY2018 (36)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	02MAY2018 (29)	09MAY2018 (36)	Grade 3	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCAEMIA	14MAY2018 (41)	14MAY2018 (41)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Blood urea increased / INCREASED UREA LEVEL	14MAY2018 (41)	04JUN2018 (62)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Intervertebral disc disorder / LUMBAR SPINE LESIONS	16MAY2018 (43)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS -OTHER, RIGHT SIDED SCAPULA PAIN.	17JUN2018 (75)		Grade 2	Not Resolved	None; Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0001	PlaceboPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED.	04JUL2018 (92)	11JUL2018 (99)	Grade 3	Resolved	None	Unrelated / Unrelated / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL.	07JUL2018 (95)	09JUL2018 (97)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	17JUL2018 (105)	25JUL2018 (113)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	25JUL2018 (113)	01AUG2018 (120)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	01AUG2018 (120)	27AUG2018 (146)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01AUG2018 (120)		Grade 3	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Lethargy / LETHARGY	03AUG2018 (122)		Grade 2	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0001	PlaceboPemPlatinum	Yes	Investigations / Weight decreased / WEIGHT LOSS	06AUG2018 (125)		Grade 1	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / PAIN IN CHEST WALL.	06AUG2018 (125)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCAEMIA	07AUG2018 (126)	07AUG2018 (126)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCAEMIA	28AUG2018 (147)	28AUG2018 (147)	Grade 3	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	28AUG2018 (147)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0202-0002	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	14SEP2018 (3)	19SEP2018 (8)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	16SEP2018 (5)	21SEP2018 (10)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	18SEP2018 (7)	19SEP2018 (8)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	19SEP2018 (8)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / PYREXIA	20SEP2018 (9)	20SEP2018 (9)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS (HEAD AND NECK)	20SEP2018 (9)	22SEP2018 (11)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Neck pain / PAIN IN LEFT SIDE OF NECK	07OCT2018 (26)	22OCT2018 (41)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS - RIGHT SIDE OF SCALP	07OCT2018 (26)		Grade 1	Ongoing	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0002	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	31OCT2018 (50)	07NOV2018 (57)	Grade 1	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED.	07NOV2018 (57)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	08NOV2018 (58)	15NOV2018 (65)	Grade 1	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Drug Withdrawn	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	15NOV2018 (65)	26NOV2018 (76)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	22NOV2018 (72)	26NOV2018 (76)	Grade 2	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	22NOV2018 (72)		Grade 1	Ongoing	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / MACULOPAPULAR RASH	08JAN2019 (119)		Grade 1	Not Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	13JAN2019 (124)	14JAN2019 (125)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
0202-0003	ADIPemPlatinum	Yes	Vascular disorders / Hot flush / HOT FLUSH	22MAY2019 (2)	22MAY2019 (2)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	24MAY2019 (4)		Grade 1	Ongoing	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Peripheral swelling / LEFT LOWER LEG SWELLING/REDNESS	01JUN2019 (12)	17JUN2019 (28)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Lymphocyte count decreased / DECREASED LYMPHOCYTE COUNT	10JUN2019 (21)	17JUN2019 (28)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHIL COUNT	10JUN2019 (21)	17JUN2019 (28)	Grade 3	Resolved	Other: TREATMENT DELAYED FOR ONE WEEK.	Possibly / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0003	ADIPemPlatinum	Yes	Investigations / Platelet count decreased / DECREASED PLATELETS	10JUN2019 (21)	17JUN2019 (28)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / White blood cell count decreased / DECREASED WHITE BLOOD CELL COUNT	10JUN2019 (21)	17JUN2019 (28)	Grade 2	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Hallucination / HALLUCINATIONS	19JUN2019 (30)	02JUL2019 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHIL COUNT	08JUL2019 (49)	15JUL2019 (56)	Grade 3	Resolved	Other: TREATMENT DELAYED FOR ONE WEEK.	Possibly / Probably / Probably / Not Applicable	Drug Interrupted / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Missing	No
			Psychiatric disorders / Hallucination / HALLUCINATIONS	18JUL2019 (59)	19JUL2019 (60)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Hallucination / HALLUCINATIONS	31JUL2019 (72)	30AUG2019 (102)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / INTERMITTENT VOMITING	20AUG2019 (92)	30AUG2019 (102)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	23AUG2019 (95)	30AUG2019 (102)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / DECREASED NEUTROPHIL COUNT	16SEP2019 (119)	23SEP2019 (126)	Grade 3	Resolved	Other: TREATMENT DELAYED FOR ONE WEEK.	Possibly / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	16SEP2019 (119)	30JAN2020 (255)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypertension / HYPERTENSION	24SEP2019 (127)	30APR2020 (346)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Injection site reaction / INJECTION SITE REACTION	18OCT2019 (151)	28OCT2019 (161)	Grade 1	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Vascular disorders / Hot flush / HOT FLUSH	28OCT2019 (161)	30OCT2019 (163)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	26NOV2019 (190)	15JAN2020 (240)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Missing / Missing	No
0202-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / ANKLE OEDEMA	12MAY2019 (5)	14MAY2019 (7)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Headache / HEADACHE	12MAY2019 (5)	14MAY2019 (7)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	12MAY2019 (5)	16SEP2019 (132)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Stomatitis / ORAL MUCOSITIS	22MAY2019 (15)	25MAR2020 (323)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Conjunctivitis / EYE BURNING (CONJUNCTIVITIS)	31MAY2019 (24)	02JUN2019 (26)	Grade 1	Resolved	None	Unlikely / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / SCALP RASH	01JUN2019 (25)	11JUN2019 (35)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01JUN2019 (25)	25MAR2020 (323)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Hot flush / HOT FLASH	02JUN2019 (26)	03JUN2019 (27)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	05JUN2019 (29)	12JUN2019 (36)	Grade 3	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL COUNT DECREASED	05JUN2019 (29)	12JUN2019 (36)	Grade 3	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	12JUN2019 (36)	17JUN2019 (41)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Lymphocyte count decreased / DECREASED LYMPHOCYTE COUNT	12JUN2019 (36)	17JUN2019 (41)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Investigations / Platelet count decreased / DECREASED PLATELETS	12JUN2019 (36)	17JUN2019 (41)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL COUNT DECREASED	12JUN2019 (36)	17JUN2019 (41)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	17JUN2019 (41)	03JUL2019 (57)	Grade 2	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / White blood cell count decreased / WHITE BLOOD CELL COUNT DECREASED	17JUN2019 (41)	03JUL2019 (57)	Grade 2	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCEMIA	17JUN2019 (41)	03JUL2019 (57)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Lymphocyte count decreased / DECREASED LYMPHOCYTE COUNT	17JUN2019 (41)	29JUL2020 (449)	Grade 2	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	19JUN2019 (43)	07SEP2019 (123)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Vascular disorders / Flushing / FACIAL FLUSHING	20JUN2019 (44)	25JUN2019 (49)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash / SCALP RASH	25JUN2019 (49)	29JUN2019 (53)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Hot flush / HOT FLASH	26JUN2019 (50)	27JUN2019 (51)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hot flush / HOT FLUSH	03JUL2019 (57)	03JUL2019 (57)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Platelet count decreased / DECREASED PLATELETS	03JUL2019 (57)	08JUL2019 (62)	Grade 1	Resolved	None	Possibly / Probably / Probably / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hot flush / HOT FLUSH	10JUL2019 (64)	19JUL2019 (73)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Oedema peripheral / ANKLE OEDEMA	11JUL2019 (65)	24APR2021 (718)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Vascular disorders / Hot flush / HOT FLASH	17JUL2019 (71)		Grade 1	Not Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	27JUL2019 (81)	28JUL2019 (82)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19AUG2019 (104)	04SEP2019 (120)	Grade 2	Resolved		Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Hypertension / HYPERTENSION	21SEP2019 (137)	02OCT2019 (148)	Grade 3	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Hypertension / HYPERTENSION	02OCT2019 (148)	09OCT2019 (155)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Hypertension / HYPERTENSION	09OCT2019 (155)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Urinary tract pain / URINARY TRACT PAIN	05NOV2019 (182)	10NOV2019 (187)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	08NOV2019 (185)	14NOV2019 (191)	Grade 2	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	07DEC2019 (214)	20DEC2019 (227)	Grade 2	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN - LEFT CHEST	23DEC2019 (230)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Osteoarthritis / ARTHRITIS RIGHT FOOT	01JUL2020 (421)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCAEMIA	12AUG2020 (463)	09SEP2020 (491)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			General disorders and administration site conditions / Oedema peripheral / OEDEMA LIMBS (RIGHT LOWER LEG)	28SEP2020 (510)	04NOV2020 (547)	Grade 1	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / OEDEMA LIMBS (RIGHT LOWER LEG)	04NOV2020 (547)	20NOV2020 (563)	Grade 2	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Injury, poisoning and procedural complications / Synovial rupture / MUSCOLOSKELETAL AND CONNECTIVE TISSUE DISORDER, RUPTURED BAKER'S CYST	04NOV2020 (547)	20NOV2020 (563)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Vascular disorders / Haematoma / HAEMATOMA (RELATED TO BAKER'S CYST)	04NOV2020 (547)	20NOV2020 (563)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypercalcaemia / HYPERCALCEMIA	04NOV2020 (547)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Injury, poisoning and procedural complications / Synovial rupture / MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS, RUPTURED BAKERS CYST	20NOV2020 (563)	14DEC2020 (587)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0004	ADIPemPlatinum	Yes	Vascular disorders / Haematoma / HAEMATOMA (RELATED TO BAKERS CYST)	20NOV2020 (563)	14DEC2020 (587)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			General disorders and administration site conditions / Oedema peripheral / OEDEMA LIMBS (RIGHT LOWER LEG)	20NOV2020 (563)		Grade 1	Resolving	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
0202-0005	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	18NOV2019 (6)	01JAN2020 (50)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	18NOV2019 (6)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTAXIS	19NOV2019 (7)	30NOV2019 (18)	Grade 1	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	20NOV2019 (8)	09FEB2020 (89)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0005	PlaceboPemPlatinum	Yes	Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	02DEC2019 (20)	13JAN2020 (62)	Grade 2	Resolved with Sequelae	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Eye disorders / Lacrimation increased / WATERING EYE	04DEC2019 (22)	25MAR2020 (134)	Grade 1	Resolved	None	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Aortic thrombosis / THROMBOEMBOLIC EVENT AORTIC THROMBUS	30DEC2019 (48)		Grade 3	Ongoing	Medication; Other: CISPLATIN WITHDRAWN	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed; Drug Withdrawn / Not Applicable	No
			Vascular disorders / Intermittent claudication / CLAUDICATIONS	06JAN2020 (55)	20JAN2020 (69)	Grade 2	Resolved with Sequelae	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	06JAN2020 (55)	31JAN2020 (80)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	06JAN2020 (55)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	13JAN2020 (62)	20JAN2020 (69)	Grade 3	Resolved	Other: TREATMENT DELAYED FOR 1 WEEK.	Unrelated / Unrelated / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0005	PlaceboPemPlatinum	Yes	Vascular disorders / Intermittent claudication / CLAUDICATIONS	20JAN2020 (69)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31JAN2020 (80)		Grade 1	Ongoing	None	Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Dizziness / DIZZINESS	05FEB2020 (85)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISMS	19FEB2020 (99)		Grade 3	Resolving	Medication	Possibly / Possibly / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	24FEB2020 (104)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	23MAR2020 (132)	14APR2020 (154)	Grade 1	Resolved with	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	15APR2020 (155)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0005	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	12MAY2020 (182)	13MAY2020 (183)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable	Yes
0202-0007	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANAEMIA	08FEB2021 (6)	15FEB2021 (13)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	15FEB2021 (13)	01MAR2021 (27)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	16FEB2021 (14)	16FEB2021 (14)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / COUGH (PRODUCTIVE)	16FEB2021 (14)	11MAR2021 (37)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINIA	22FEB2021 (20)	29MAR2021 (55)	Grade 3	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	01MAR2021 (27)	08MAR2021 (34)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0007	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	04MAR2021 (30)	11MAR2021 (37)	Grade 2	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Fall / FALL	05MAR2021 (31)	05MAR2021 (31)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	08MAR2021 (34)	29MAR2021 (55)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALAEMIA	09MAR2021 (35)	11MAR2021 (37)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood urea increased / INCREASED SERUM UREA	09MAR2021 (35)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	09MAR2021 (35)		Grade 3	Not Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12MAR2021 (38)		Grade 1	Ongoing	Medication	Unrelated / Definitely / Not Applicable / Definitely	Not Applicable / Not Applicable / Not Applicable / Unknown	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0202-0007	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	12MAR2021 (38)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Withdrawn / Not Applicable / Not Applicable / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	29MAR2021 (55)	29MAR2021 (55)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	29MAR2021 (55)		Grade 1	Ongoing	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	29MAR2021 (55)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
0203-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	14DEC2017 (10)	17DEC2017 (13)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hypoxia / HYPOXIA	24JAN2018 (51)	29JAN2018 (56)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	24JAN2018 (51)	14FEB2018 (72)	Grade 2	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	21MAR2018 (107)	27MAR2018 (113)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable	No
			Neoplasms benign, malignant and unspecified (incl cysts and polyps) / Bone cancer metastatic / HYPERCALCAEMIA SECONDARY TO METASTATIC BONE LESIONS	21MAR2018 (107)	27MAR2018 (113)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Not Applicable / Not Applicable	No
0203-0002	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH ON HEAD	04JAN2018 (3)	10JAN2018 (9)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON NECK	04JAN2018 (3)	10JAN2018 (9)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Dyspepsia / WORSENING INDIGESTION	07JAN2018 (6)		Grade 2	Not Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	07JAN2018 (6)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITTING	16FEB2018 (46)	16FEB2018 (46)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0203-0004	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	01MAR2018 (9)	16MAR2018 (24)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	14MAR2018 (22)	21MAR2018 (29)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Drug Interrupted	No
			Skin and subcutaneous tissue disorders / Rash / RASH	06APR2018 (45)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / BREATHING DIFFICULTY	09APR2018 (48)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0203-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITTING	07APR2018 (4)	10APR2018 (7)	Grade 2	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	08MAY2018 (35)	11MAY2018 (38)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITTING	08MAY2018 (35)	11MAY2018 (38)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Hyperhidrosis / SWEATING	16MAY2018 (43)		Grade 1	Ongoing	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHIL COUNT	23MAY2018 (50)	30MAY2018 (57)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02JUN2018 (60)	09JUN2018 (67)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITTING	02JUN2018 (60)	09JUN2018 (67)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	13JUN2018 (71)	29JUN2018 (87)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	18JUL2018 (106)		Grade 2	Not Resolved	Medication	Unrelated / Unlikely / Probably / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Missing	No
			Psychiatric disorders / Insomnia / INSOMNIA	05AUG2018 (124)		Grade 1	Ongoing	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	05SEP2018 (155)		Grade 1	Ongoing	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0203-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Pneumonia / COMMUNITY ACQUIRED PNEUMONIA	08MAY2018 (7)	11MAY2018 (10)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Reduced / Drug Interrupted / Not Applicable	No
			Infections and infestations / Pneumonia / COMMUNITY ACQUIRED PNEUMONIA	12MAY2018 (11)	14MAY2018 (13)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALAEMIA	13MAY2018 (12)	16MAY2018 (15)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0008	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / INDIGESTION	10AUG2018 (3)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Acarodermatitis / SCABIES	28AUG2018 (21)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14SEP2018 (38)	23SEP2018 (47)	Grade 1	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / ITCHY SKIN	25OCT2018 (79)	25OCT2018 (79)	Grade 1	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Flushing / FLUSHED	25OCT2018 (79)	25OCT2018 (79)	Grade 1	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0203-0009	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH	05SEP2018 (8)	12SEP2018 (15)	Grade 1	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	19SEP2018 (22)	21SEP2018 (24)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0009	PlaceboPemPlatinum	Yes	Infections and infestations / Lower respiratory tract infection / LOWER RESPIRATORY TRACT INFECTION	19SEP2018 (22)	21SEP2018 (24)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESAEMIA	19SEP2018 (22)	21SEP2018 (24)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	04OCT2018 (37)	11OCT2018 (44)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	13OCT2018 (46)	14OCT2018 (47)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Dose Not Changed / Not Applicable	Yes
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	24OCT2018 (57)	31OCT2018 (64)	Grade 3	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	07NOV2018 (71)	23FEB2019 (179)	Grade 2	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Pain in extremity / PAIN IN RIGHT SHOULDER TO ARM	07NOV2018 (71)	23FEB2019 (179)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0009	PlaceboPemPlatinum	Yes	Psychiatric disorders / Confusional state / CONFUSION	30JAN2019 (155)	23FEB2019 (179)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Possibly / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes
0203-0010	ADIPemPlatinum	Yes	Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY STAGE 1	24JAN2019 (16)	05FEB2019 (28)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Withdrawn / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	28JAN2019 (20)	02FEB2019 (25)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Infections and infestations / Neutropenic sepsis / NEUTROPENIC SEPSIS	30JAN2019 (22)	02FEB2019 (25)	Grade 4	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	31JAN2019 (23)	05FEB2019 (28)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
0203-0013	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	10APR2019 (29)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed; Drug Interrupted / Dose Not Changed; Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0013	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	24APR2019 (43)	01MAY2019 (50)	Grade 3	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Investigations / Platelet count decreased / DECREASED PLATELETS	16MAY2019 (65)	22MAY2019 (71)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	22MAY2019 (71)		Grade 2	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Investigations / White blood cell count decreased / DECREASED WHITE BLOOD CELLS	22MAY2019 (71)		Grade 2	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY (NUMB FEET WHEN NECK IS BENT)	20JUL2019 (130)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31JUL2019 (141)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Hyperhidrosis / SWEATING	25SEP2019 (197)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0013	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	06APR2020 (391)	08APR2020 (393)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	07APR2020 (392)	08APR2020 (393)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
0203-0014	ADIPemPlatinum	Yes	Ear and labyrinth disorders / Tinnitus / INTERMITTENT RINGING IN BOTH EARS	25JUL2019 (2)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	14AUG2019 (22)	21AUG2019 (29)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	14DEC2019 (144)	14DEC2019 (144)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / PAIN LEFT SIDE OF RIBS FROM FALL	14DEC2019 (144)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0015	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	24SEP2019 (56)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC PAIN.	07OCT2019 (69)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	23OCT2019 (85)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / REDUCED APPETITE	13NOV2019 (106)		Grade 1	Ongoing	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0203-0016	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	27AUG2019 (7)	12NOV2019 (84)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	27AUG2019 (7)	26NOV2019 (98)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Nasopharyngitis / COLD	02SEP2019 (13)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0016	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH ON CHEST	03SEP2019 (14)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / GASTRIC REFLUX	26SEP2019 (37)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Insomnia / INSOMNIA	26SEP2019 (37)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	26SEP2019 (37)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood potassium decreased / LOW POTASSIUM	17OCT2019 (58)	27NOV2019 (99)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	22OCT2019 (63)	24OCT2019 (65)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Reproductive system and breast disorders / Prostatomegaly / SWOLLEN PROSTATE	30OCT2019 (71)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0016	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	13NOV2019 (85)		Grade 3	Ongoing	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Vomiting / VOMITING	13NOV2019 (85)		Grade 3	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	13NOV2019 (85)		Grade 3	Ongoing	None	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	13NOV2019 (85)		Grade 3	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Oral pain / SORE MOUTH	23NOV2019 (95)		Grade 1	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / INTERMITTENT DIARRHOEA	27NOV2019 (99)		Grade 1	Ongoing	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	04DEC2019 (106)		Grade 1	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0016	PlaceboPemPlatinum	Yes	Nervous system disorders / Cerebrovascular accident / STROKE	28JAN2020 (161)	28FEB2020 (192)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unlikely / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Missing	Yes
0203-0018	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	21JAN2020 (7)		Grade 3	Ongoing	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	Yes
			Nervous system disorders / Cerebrovascular accident / STROKE	07FEB2020 (24)	13FEB2020 (30)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Unlikely / Unlikely / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Missing	Yes
0203-0019	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	16DEC2020 (1)	18DEC2020 (3)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / SHOULDER PAIN	22DEC2020 (7)		Grade 2	Resolving	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	31DEC2020 (16)	02JAN2021 (18)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0203-0019	ADIPemPlatinum	Yes	Psychiatric disorders / Confusional state / CONFUSION	31DEC2020 (16)	02JAN2021 (18)	Grade 2	Resolved	None	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable	No
0204-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	17MAY2018 (2)	22MAY2018 (7)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	19MAY2018 (4)	23MAY2018 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	21MAY2018 (6)	22MAY2018 (7)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	21MAY2018 (6)	22MAY2018 (7)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	25MAY2018 (10)	28JUN2018 (44)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	25MAY2018 (10)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0001	PlaceboPemPlatinum	Yes	Eye disorders / Vitreous floaters / OCULAR FLOATERS	08JUN2018 (24)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	30AUG2018 (107)		Grade 2	Not Resolved	Other: CHANGED CISPLATIN TO CARBOPLATIN	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Dose Not Changed	No
0204-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	13JUL2018 (3)	19JUL2018 (9)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Ear and labyrinth disorders / Tinnitus / TINNITUS	14JUL2018 (4)	23AUG2018 (44)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYPNEA	16JUL2018 (6)	19JUL2018 (9)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	18JUL2018 (8)	28DEC2018 (171)	Grade 3	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Drug Withdrawn / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0002	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	02AUG2018 (23)	08AUG2018 (29)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	02AUG2018 (23)	09AUG2018 (30)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	09AUG2018 (30)	17AUG2018 (38)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	09AUG2018 (30)	23AUG2018 (44)	Grade 2	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	09AUG2018 (30)	28DEC2018 (171)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	09AUG2018 (30)	28DEC2018 (171)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	23AUG2018 (44)	30AUG2018 (51)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0003	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	01AUG2018 (1)	29AUG2018 (29)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	01AUG2018 (1)		Grade 2	Not Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	09AUG2018 (9)	25NOV2018 (117)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	29AUG2018 (29)	30AUG2018 (30)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	29AUG2018 (29)	30AUG2018 (30)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
0204-0004	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	24AUG2018 (4)	02SEP2018 (13)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dysphonia / HOARSENESS	24AUG2018 (4)	08NOV2018 (80)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA (INTERMITTENT)	24AUG2018 (4)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA (INCREASED FROM MEDHX - INTERMITTENT)	24AUG2018 (4)		Grade 2	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN (INCREASED FROM MEDHX)	26AUG2018 (6)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / METALLIC TASTE IN MOUTH	02SEP2018 (13)	20SEP2018 (31)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02SEP2018 (13)		Grade 2	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	10SEP2018 (21)	08NOV2018 (80)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0004	PlaceboPemPlatinum	Yes	Nervous system disorders / Dysgeusia / METALLIC TASTE IN MOUTH	21SEP2018 (32)		Grade 2	Not Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye pain / STINGING EYES	25SEP2018 (36)		Grade 2	Not Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0204-0005	ADIPemPlatinum	Yes	Nervous system disorders / Headache / HEADACHE	22SEP2018 (4)	24SEP2018 (6)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	22SEP2018 (4)		Grade 2	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / TASTE CHANGE	22SEP2018 (4)		Grade 2	Unknown	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	22SEP2018 (4)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	23SEP2018 (5)	24SEP2018 (6)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0005	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION	23SEP2018 (5)	24SEP2018 (6)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Investigations / Blood creatinine increased / CREATININE INCREASED	22NOV2018 (65)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Pain / PAIN	13DEC2018 (86)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	01JAN2019 (105)	03JAN2019 (107)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Immune system disorders / Drug hypersensitivity / ALLERGIC REACTION TO STUDY DRUG	28JUN2019 (283)	29JUN2019 (284)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
0204-0006	ADIPemPlatinum	Yes	Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEPHROPATHY (INTERMITTENT)	05DEC2018 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	21MAR2019 (107)	02APR2019 (119)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Not Applicable / Drug Withdrawn / Not Applicable	Yes
0204-0007	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	02FEB2019 (4)	07FEB2019 (9)	Grade 2	Resolved	None	Definitely / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	03FEB2019 (5)	07FEB2019 (9)	Grade 2	Resolved	None	Definitely / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	05FEB2019 (7)	13FEB2019 (15)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	08FEB2019 (10)		Grade 1	Ongoing	None	Definitely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Pancreatitis / GALLSTONE PANCREATITIS	06MAR2019 (36)	07MAR2019 (37)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	18MAR2019 (48)		Grade 2	Ongoing	Medication	Definitely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMITING	04APR2019 (65)	25APR2019 (86)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Lymphadenopathy / GENERAL DISORDERS OTHER - SWELLING SUPRACLAVICULAR LYMPH NODES	10MAY2019 (101)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0204-0008	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	15FEB2019 (10)	08MAR2019 (31)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	04MAR2019 (27)	28MAR2019 (51)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	29MAR2019 (52)		Grade 1	Unknown	Medication	Unrelated / Definitely / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0008	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	02MAY2019 (86)		Grade 1	Unknown	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	26SEP2019 (233)		Grade 2	Unknown	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0204-0009	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	08MAR2019 (3)	13MAR2019 (8)	Grade 1	Resolved with Sequelae	None	Unlikely / Definitely / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Dermatitis acneiform / ACNEIFORM RASH OVER UPPER CHEST	11MAR2019 (6)		Grade 1	Ongoing	None	Unlikely / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	28MAR2019 (23)	04APR2019 (30)	Grade 3	Resolved	None	Unrelated / Definitely / Definitely / Definitely	Dose Not Changed / Drug Interrupted / Drug Interrupted / Drug Interrupted	No
			Investigations / Weight decreased / WEIGHT LOSS	29MAR2019 (24)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0009	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	04APR2019 (30)	10APR2019 (36)	Grade 2	Resolved	Medication	Unlikely / Definitely / Definitely / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	10APR2019 (36)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	01MAY2019 (57)	02MAY2019 (58)	Grade 3	Resolved	Medication; Withdrawal from Study	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Vomiting / VOMITING	01MAY2019 (57)	02MAY2019 (58)	Grade 3	Resolved	Medication; Withdrawal from Study	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain upper / STOMACH PAIN	01MAY2019 (57)	23MAY2019 (79)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	29MAY2019 (85)	30MAY2019 (86)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	Yes
			Gastrointestinal disorders / Vomiting / VOMITING	29MAY2019 (85)	30MAY2019 (86)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0009	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Stomatitis / MUCOSITIS (ORAL)	29MAY2019 (85)		Grade 2	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	18JUN2019 (105)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
0204-0010	ADIPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain upper / RIGHT UPPER QUADRANT PAIN	15AUG2019 (9)	17AUG2019 (11)		Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	15AUG2019 (9)	17AUG2019 (11)	Grade 3	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	15AUG2019 (9)	17AUG2019 (11)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	15AUG2019 (9)	18AUG2019 (12)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0010	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pain / CHRONIC PAIN	31OCT2019 (86)	07NOV2019 (93)	Grade 3	Resolved	Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
0204-0011	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	21SEP2019 (4)		Grade 1	Ongoing	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	02OCT2019 (15)	04OCT2019 (17)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	13OCT2019 (26)	16OCT2019 (29)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Nasopharyngitis / COUGH AND COLD	11NOV2019 (55)			Unknown	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	15NOV2019 (59)	21NOV2019 (65)	Grade 3	Resolved	Other: RBC TRANSFUSION	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0204-0011	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	15NOV2019 (59)	21NOV2019 (65)	Grade 3	Resolved		Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	15NOV2019 (59)	21NOV2019 (65)	Grade 1	Resolved		Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	12DEC2019 (86)	09JAN2020 (114)	Grade 3	Resolved	Other: RBC TRANSFUSION	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0205-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	07JUL2018 (5)	05AUG2018 (34)	Grade 1	Resolved	None	Possibly / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye disorder / EYE DISORDER (OTHER)	18JUL2018 (16)	29JUL2018 (27)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	24JUL2018 (22)	25JUL2018 (23)	Grade 4	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LEFT SIDED BACK PAIN	31JUL2018 (29)	08AUG2018 (37)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0001	ADIPemPlatinum	Yes	Renal and urinary disorders / Pollakiuria / URINARY FREQUENCY	31JUL2018 (29)	08AUG2018 (37)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	07SEP2018 (67)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye discharge / EYE DISORDER (OTHER)STICKY EYES	22SEP2018 (82)	26SEP2018 (86)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye discharge / EYE DISORDER OTHER (STICKY EYES, BOTH)	13OCT2018 (103)	15OCT2018 (105)	Grade 1	Resolved	None	Unlikely / Definitely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Eye discharge / EYE DISORDER OTHER - STICKY EYES	22OCT2018 (112)	24OCT2018 (114)	Grade 1	Resolved	None	Unlikely / Possibly / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Eye disorders / Eye discharge / EYE DISORDER OTHER - STICKY EYES	01NOV2018 (122)	04NOV2018 (125)	Grade 1	Resolved	None	Unlikely / Possibly / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	05NOV2018 (126)	05NOV2018 (126)	Grade 1	Resolved	None	Unlikely / Possibly / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0001	ADIPemPlatinum	Yes	Eye disorders / Eye discharge / EYE DISORDER OTHER - STICKY EYES	17NOV2018 (138)	19NOV2018 (140)	Grade 1	Resolved	None	Unlikely / Possibly / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	03JAN2019 (185)	04JAN2019 (186)	Grade 1	Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	05JAN2019 (187)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Ear and labyrinth disorders / Inner ear disorder / EAR AND LABYRINTH DISORDER	14JAN2019 (196)	17JAN2019 (199)	Grade 1	Resolved	Other: PATIENT IS DUE TO GET EARS SYRINGED TO REMOVE EAR WAX	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY IN BOTH HANDS, INDEX AND THUMB	05FEB2019 (218)		Grade 1	Not Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Eye disorders / Vitreous floaters / BILATERAL EYE FLOATERS	23FEB2019 (236)		Grade 2	Not Resolved	Other: REFERRED TO OPTICIANS	Unlikely / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0001	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	03MAR2019 (244)	11MAR2019 (252)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0205-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	19APR2019 (5)	15MAY2019 (31)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	21APR2019 (7)	22APR2019 (8)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Vascular disorders / Hypertension / HYPERTENSION	16MAY2019 (32)		Grade 2	Not Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / PAIN (BACK RIGHT SIDE)	24MAY2019 (40)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / GASTRIC REFLUX	29MAY2019 (45)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	05JUN2019 (52)	11JUN2019 (58)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0002	PlaceboPemPlatinum	Yes	Nervous system disorders / Hypoaesthesia / RIGHT SIDED CHEST NUMBNESS (INTERMITTENT)	27JUN2019 (74)		Grade 1	Not Resolved	Other: CISPLATIN STOPPED PATIENT COMMENCE D ON CARBOPLATIN	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	10JUL2019 (87)		Grade 2	Not Resolved	Other: CISPLATIN STOPPED	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Dose Not Changed	No
0205-0005	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	30AUG2019 (4)	05SEP2019 (10)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash / SKIN RASH RIGHT TEMPLE AND BEHIND EAR	31AUG2019 (5)	25SEP2019 (30)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	01SEP2019 (6)	04SEP2019 (9)	Grade 1	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0005	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Sinus pain / SINUS PAIN	17SEP2019 (22)	19SEP2019 (24)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Vomiting / VOMITING	18SEP2019 (23)	18SEP2019 (23)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	21SEP2019 (26)	25SEP2019 (30)	Grade 1	Resolved		Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	21SEP2019 (26)	05OCT2019 (40)	Grade 2	Resolved	Medication	Unrelated /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	26SEP2019 (31)	27OCT2019 (62)	Grade 2	Resolved	Medication	Unrelated /	Dose Not Changed /	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	26SEP2019 (31)		Grade 2	Not Resolved	Medication	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	06OCT2019 (41)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0205-0005	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / INCREASED SHORTNESS OF BREATH	24OCT2019 (59)	28OCT2019 (63)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	27OCT2019 (62)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	04NOV2019 (70)	05NOV2019 (71)	Grade 1	Resolved	None	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0205-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Pneumonia / PNEUMONIA	26OCT2019 (5)	04NOV2019 (14)	Grade 4	Resolved	Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unlikely / Probably / Probably / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
			Infections and infestations / Oral candidiasis / ORAL THRUSH	01NOV2019 (11)	07NOV2019 (17)	Grade 2	Resolved	Medication	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
0207-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	20SEP2018 (4)	21SEP2018 (5)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	20SEP2018 (4)	21SEP2018 (5)	Grade 1	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / RIGHT CHEST PAIN NON CARDIAC	22SEP2018 (6)		Grade 2	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Nervous system disorders / Lethargy / LETHARGY	23SEP2018 (7)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Neutropenic sepsis / NEUTROPENIC SEPSIS	28SEP2018 (12)	30SEP2018 (14)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Possibly / Definitely / Definitely / Not Applicable	Drug Interrupted; Drug Withdrawn / Drug Interrupted / Dose Not Changed / Not Applicable	Yes
0207-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	01DEC2018 (5)		Grade 2	Ongoing	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	01DEC2018 (5)		Grade 1	Not Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	02DEC2018 (6)	02DEC2018 (6)	Grade 2	Resolved	None	Unlikely / Definitely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02DEC2018 (6)	18DEC2018 (22)	Grade 2	Resolved	Medication	Unlikely / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER	04DEC2018 (8)	13DEC2018 (17)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Sepsis / OCCULT SEPSIS	04DEC2018 (8)	14DEC2018 (18)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Investigations / Hepatic enzyme increased / RAISED LIVER ENZYMES	05DEC2018 (9)	15DEC2018 (19)	Grade 2	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESAEMIA	10DEC2018 (14)	11DEC2018 (15)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypophosphataemia / HYPOPHOSPHATAEMIA	10DEC2018 (14)	11DEC2018 (15)	Grade 1	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / BILATERAL ANKLE OEDEMA	12DEC2018 (16)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / EXACERBATION OF DYSPNEA	19DEC2018 (23)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	29DEC2018 (33)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0207-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	13JUL2019 (6)	18JUL2019 (11)	Grade 2	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY TRACT INFECTION	13JUL2019 (6)	19JUL2019 (12)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Lethargy / LETHARGY	15JUL2019 (8)	16JUL2019 (9)	Grade 3	Resolved	None	Possibly / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	15JUL2019 (8)	17JUL2019 (10)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17JUL2019 (10)	18JUL2019 (11)	Grade 2	Resolved	None	Possibly / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATRAEMIA	17JUL2019 (10)	19JUL2019 (12)	Grade 3	Resolved	None	Possibly / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL CANDIDIASIS	17JUL2019 (10)	24JUL2019 (17)	Grade 1	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	19JUL2019 (12)	20JUL2019 (13)	Grade 1	Resolved	Medication	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	19JUL2019 (12)	25AUG2019 (49)	Grade 1	Resolved	None	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	19JUL2019 (12)	26AUG2019 (50)	Grade 1	Resolved	None	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0003	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hyponatraemia / HYPONATRAEMIA	19JUL2019 (12)		Grade 1	Not Resolved	None	Possibly / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	01AUG2019 (25)	05AUG2019 (29)	Grade 1	Resolved	Medication	Possibly / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	06AUG2019 (30)	10AUG2019 (34)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	20AUG2019 (44)		Grade 2	Not Resolved	Other: BLOOD TRANSFUSION	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	26AUG2019 (50)		Grade 2	Not Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / INCREASED DYSPNEA	29AUG2019 (53)	05SEP2019 (60)	Grade 3	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION	03SEP2019 (58)	06SEP2019 (61)	Grade 3	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0003	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / INCREASED DYSPNEOA	05SEP2019 (60)	11SEP2019 (66)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Infections and infestations / Pleural infection / PLEURAL INFECTION	06SEP2019 (61)		Grade 3	Ongoing	Medication	Unrelated /	Dose Not Changed /	Yes
			Nervous system disorders / Lethargy / LETHARGY	11SEP2019 (66)		Grade 1	Not Resolved	None	Unrelated /	Dose Not Changed /	No
0207-0004	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	07JAN2020 (2)		Grade 1	Not Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	08JAN2020 (3)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	11JAN2020 (6)	18JAN2020 (13)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated /	Dose Not Changed /	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	11JAN2020 (6)	18JAN2020 (13)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0004	PlaceboPemPlatinum	Yes	Psychiatric disorders / Confusional state / CONFUSION	12JAN2020 (7)	13JAN2020 (8)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / PLEURITIC CHEST PAIN	12JAN2020 (7)	13JAN2020 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12JAN2020 (7)	18JAN2020 (13)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / RAISED CREATININE	28JAN2020 (23)	04FEB2020 (30)	Grade 1	Resolved	Other: CISPLATIN DECREASED	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Joint swelling / SWOLLEN ANKLE	30JAN2020 (25)	10FEB2020 (36)	Grade 1	Resolved	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Oedema peripheral / BILATERAL LEG OEDEMA	30JAN2020 (25)		Grade 1	Ongoing	None	Possibly / Possibly / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31JAN2020 (26)	13MAR2020 (68)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	31JAN2020 (26)		Grade 1	Ongoing	None	Possibly / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02FEB2020 (28)	02FEB2020 (28)	Grade 1	Resolved	None	Probably / Probably / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	05FEB2020 (31)	16FEB2020 (42)	Grade 3	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed; Drug Interrupted / Dose Reduced; Drug Interrupted / Dose Not Changed / Not Applicable	No
			Infections and infestations / Pharyngitis / THROAT INFECTION	12FEB2020 (38)	19FEB2020 (45)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	16FEB2020 (42)	14MAR2020 (69)	Grade 1	Resolved	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	25FEB2020 (51)	03MAR2020 (58)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0207-0004	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / EXACERBATION OF DYSPNEOA	13MAR2020 (68)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14MAR2020 (69)		Grade 2	Ongoing	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	17MAR2020 (72)	19MAR2020 (74)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Vascular disorders / Deep vein thrombosis / DEEP VENOUS THROMBOSIS	17MAR2020 (72)		Grade 2	Ongoing	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
0208-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	17MAY2018 (4)	20AUG2018 (99)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	18MAY2018 (5)	22MAY2018 (9)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / INTERMITTENT INDIGESTION	23MAY2018 (10)	22AUG2018 (101)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Oral pain / SORE MOUTH	23MAY2018 (10)		Grade 2	Ongoing	Medication	Unrelated / Probably / Probably / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dysphonia / HOARSENESS	23MAY2018 (10)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON FEET	01JUN2018 (19)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	15JUN2018 (33)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	25JUN2018 (43)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Vascular disorders / Deep vein thrombosis / LEFT FEMORAL DEEP VEIN THROMBOSIS	25JUN2018 (43)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0001	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH ON FACE	15JUL2018 (63)	31AUG2018 (110)	Grade 2	Resolved	Medication	Possibly / Unrelated / Possibly / Unrelated	Drug Interrupted / Dose Not Changed / Dose Not Changed /	No
			Investigations / Blood glucose increased / RAISED BLOOD GLUCOSE	13AUG2018 (92)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20AUG2018 (99)		Grade 2	Ongoing	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash macular / RED AREA ON BUTTOCKS	30AUG2018 (109)		Grade 2	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	31AUG2018 (110)	04SEP2018 (114)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	31AUG2018 (110)	05NOV2018 (176)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH	01SEP2018 (111)		Grade 3	Ongoing	Medication	Probably / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0001	ADIPemPlatinum	Yes	Infections and infestations / Pneumonia / PNEUMONIA	12SEP2018 (122)	18SEP2018 (128)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORT OF BREATH	12SEP2018 (122)		Grade 1	Ongoing	Other: DRUG INTERRUPTED	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	15OCT2018 (155)	25OCT2018 (165)	Grade 2	Resolved	Medication	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Unknown / Not Applicable	No
			Metabolism and nutrition disorders / Gout / GOUT	09NOV2018 (180)	10NOV2018 (181)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	16NOV2018 (187)		Grade 2	Ongoing	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / PAIN - RIGHT LOWER RIBS	26NOV2018 (197)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
0208-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	06SEP2018 (3)	06DEC2018 (94)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0002	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION	09SEP2018 (6)	11SEP2018 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Mouth ulceration / MOUTH ULCERATION	23SEP2018 (20)	02OCT2018 (29)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIC	25SEP2018 (22)	01OCT2018 (28)	Grade 4	Resolved	None	Definitely / Definitely / Definitely / Definitely	Drug Interrupted / Dose Reduced / Dose Reduced / Dose Reduced	No
			Eye disorders / Vision blurred / BLURRED VISION	08OCT2018 (35)	16OCT2018 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Hyperaesthesia / SENSITIVE SKIN	10OCT2018 (37)	31OCT2018 (58)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Unknown / Unknown / Unknown / Not Applicable;	No
			Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	10OCT2018 (37)	25FEB2019 (175)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Missing / Unknown / Missing / Unknown	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIC	24OCT2018 (51)	31OCT2018 (58)	Grade 4	Resolved	None	Probably / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0002	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / PAIN IN RIGHT SHOULDER	30NOV2018 (88)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Infection / INFECTION LEFT HAND & ARM	03DEC2018 (91)		Grade 1	Ongoing	Medication	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0208-0003	ADIPemPlatinum	Yes	Product issues / Device leakage / LEAKING CHEST DRAIN	17NOV2018 (4)	23NOV2018 (10)	Grade 1	Resolved	Other: REFERRAL MADE TO RESPIRATORY TEAM TO FIX DRAIN.	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	26NOV2018 (13)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Missing / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	07DEC2018 (24)		Grade 3	Unknown	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	11DEC2018 (28)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0003	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Increased viscosity of bronchial secretion / THICK SPUTUM	13DEC2018 (30)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Fluid retention / FLUID RETENTION	24DEC2018 (41)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Cardiac arrest / CARDIAC ARREST	04JAN2019 (52)	05JAN2019 (53)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Withdrawn / Not Applicable / Drug Withdrawn / Not Applicable	Yes
0208-0004	PlaceboPemPlatinum	Yes	Nervous system disorders / Tremor / SHAKING IN HANDS	27MAR2019 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	30MAR2019 (4)		Grade 2	Ongoing	Medication	Unrelated / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	30MAR2019 (4)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / WORSENING ABDOMINAL PAIN	02APR2019 (7)	05APR2019 (10)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	Yes
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	03APR2019 (8)	03APR2019 (8)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	03APR2019 (8)	05APR2019 (10)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	05APR2019 (10)		Grade 1	Ongoing	Medication	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	24MAY2019 (59)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Dose Not Changed / Missing	No
			Investigations / Blood alkaline phosphatase increased / ALP INCREASED	24MAY2019 (59)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	No
			General disorders and administration site conditions / Pyrexia / PYREXIA	29MAY2019 (64)	03JUN2019 (69)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dysphagia / DIFFICULTY SWALLOWING	07JUN2019 (73)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	21JUN2019 (87)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / PYREXIA	03JUL2019 (99)	04JUL2019 (100)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged	Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed	Yes
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	06JUL2019 (102)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	Yes
			General disorders and administration site conditions / Non-cardiac chest pain / WORSENING LEFT CHEST WALL- NON CARDIAC	06JUL2019 (102)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	Yes
			Nervous system disorders / Monoplegia / UNABLE TO MOVE LEFT LEG	26JUL2019 (122)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	20MAY2019 (1)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	20MAY2019 (1)		Grade 1	Ongoing	Medication	Probably / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	24MAY2019 (5)	25MAY2019 (6)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	25MAY2019 (6)	26MAY2019 (7)	Grade 1	Resolved	None	Unrelated / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Neutropenic sepsis / NEUTROPENIC SEPSIS	06JUN2019 (18)	10JUN2019 (22)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			General disorders and administration site conditions / Non-cardiac chest pain / PAIN IN CHESTLEFT SIDE-NON CARDIAC	10JUN2019 (22)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	08JUL2019 (50)		Grade 2	Ongoing		Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0006	ADIPemPlatinum	Yes	Psychiatric disorders / Anxiety / ANXIETY	21JUL2019 (63)	27AUG2019 (100)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORT OF BREATH ON EXURTION	05AUG2019 (78)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	15SEP2019 (119)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0208-0007	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	14JUL2019 (5)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / REDUCED APPETITE	15JUL2019 (6)		Grade 1	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Syncope / SYNCOPÉ	17JUL2019 (8)	17JUL2019 (8)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0007	ADIPemPlatinum	Yes	Infections and infestations / Infection / SUSPECTED INFECTION	17JUL2019 (8)	18JUL2019 (9)	Grade 2	Resolved	Medication; Other: BLOOD TEST TAKEN TO ENSURE PATIENT NOT NEUTROPENIC	Unrelated / Possibly / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	17JUL2019 (8)	18JUL2019 (9)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	18JUL2019 (9)	19JUL2019 (10)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	24JUL2019 (15)	26JUL2019 (17)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Infections and infestations / Infection / SUSPECTED INFECTION	24JUL2019 (15)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	26JUL2019 (17)	29JUL2019 (20)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0007	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	26JUL2019 (17)		Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILATION	02AUG2019 (24)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Cerebrovascular accident / CVA INFARCT	07SEP2019 (60)		Grade 4	Ongoing	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Unrelated	Drug Interrupted; Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Drug Withdrawn	Yes
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	08SEP2019 (61)	09SEP2019 (62)	Grade 3	Resolved	Medication	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Tachycardia / TACHYCARDIA	08SEP2019 (61)	10SEP2019 (63)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	08SEP2019 (61)		Grade 3	Ongoing	Medication	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Dysphagia / DYSPHAGIA	09SEP2019 (62)		Grade 3	Ongoing	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0208-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	23OCT2019 (8)	23MAR2020 (160)	Grade 2	Resolved	Medication	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	23OCT2019 (8)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA LOW HEAMOGLOBIN	06NOV2019 (22)		Grade 2	Ongoing	Medication	Unrelated / Definitely / Unrelated / Definitely	Dose Not Changed / Drug Interrupted / Not Applicable / Dose Not Changed	No
			Infections and infestations / Nasopharyngitis / COLD	18DEC2019 (64)	20DEC2019 (66)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	20DEC2019 (66)		Grade 2	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0209-0001	ADIPemPlatinum	Yes	Eye disorders / Lacrimation increased / RUNNY EYES	26APR2018 (3)		Grade 1	Ongoing	Medication	Unlikely / Probably / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0001	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RUNNY NOSE	26APR2018 (3)		Grade 1	Ongoing	None	Unlikely / Probably / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	28APR2018 (5)	04MAY2018 (11)	Grade 2	Resolved	Medication; Other: ABDOMINAL X-RAY PERFORMED = NAD	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	28APR2018 (5)	04MAY2018 (11)	Grade 2	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	28APR2018 (5)	08MAY2018 (15)	Grade 1	Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LACK OF APPETITE	28APR2018 (5)	08MAY2018 (15)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	28APR2018 (5)		Grade 1	Ongoing	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0001	ADIPemPlatinum	Yes	Investigations / Blood urea increased / ELEVATED UREA	01MAY2018 (8)	05JUN2018 (43)	Grade 1	Resolved	Other: GIVEN 1 LITRE OF IV FLUIDS AND BLOODS RE-CHECKED	Unlikely / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	16MAY2018 (23)	23MAY2018 (30)	Grade 1	Resolved	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	16MAY2018 (23)	23MAY2018 (30)	Grade 2	Resolved	Medication	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Vision blurred / BLURRED EYESIGHT	21MAY2018 (28)	01AUG2018 (100)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH - LOWER ARMS	23MAY2018 (30)	03JUN2018 (41)	Grade 1	Resolved	Medication	Unlikely / Probably / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Arthralgia / PAIN IN LEFT FOOT (ARTHRITIC)	25JUN2018 (63)	11JUL2018 (79)	Grade 3	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0001	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Arthralgia / PAIN IN RIGHT WRIST (ARTHRITIC)	26JUN2018 (64)	11JUL2018 (79)	Grade 2	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Metabolism and nutrition disorders / Gout / GOUT	28JUL2018 (96)	21AUG2018 (120)	Grade 2	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Metabolism and nutrition disorders / Gout / GOUT	22AUG2018 (121)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Drug Interrupted / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / WORSENING INTERMITTENT RIGHT SIDE ANTERIOR CHEST PAIN - NON CARDIAC	13DEC2018 (234)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0209-0003	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA - WORSENING	15MAR2019 (-4)	20MAR2019 (2)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / RIGHT SHOULDER PAIN	16MAR2019 (-3)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Missing / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0003	ADIPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / RAISED ALK PHOS	18MAR2019 (-1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Unlikely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Vascular disorders / Hypertension / INTERMITTANT HYPERTENSION	19MAR2019 (1)	15MAY2019 (58)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	20MAR2019 (2)	30MAR2019 (12)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA - INTERMITTANT	21MAR2019 (3)	01MAY2019 (44)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPONEA	21MAR2019 (3)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	22MAR2019 (4)	23MAR2019 (5)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Missing / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	22MAR2019 (4)	24MAR2019 (6)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0003	ADIPemPlatinum	Yes	Ear and labyrinth disorders / Tinnitus / TINNITUS	22MAR2019 (4)	29APR2019 (42)	Grade 1	Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed; Drug Withdrawn / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	22MAR2019 (4)		Grade 1	Not Resolved	None	Unrelated / Definitely / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	24MAR2019 (6)	30MAR2019 (12)	Grade 3	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	25MAR2019 (7)	30MAR2019 (12)	Grade 2	Resolved	None	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31MAR2019 (13)	04MAY2019 (47)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Night sweats / NIGHT SWEATS	31MAR2019 (13)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02MAY2019 (45)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0003	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	05MAY2019 (48)		Grade 2	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Device related infection / INFECTION PLEUREX DRAIN SITE	15MAY2019 (58)	18JUN2019 (92)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unlikely / Not Applicable / Unlikely	Drug Withdrawn / Drug Withdrawn / Not Applicable / Drug Withdrawn	Yes
			Vascular disorders / Hypotension / HYPOTENSION INTERMITTANT	15MAY2019 (58)		Grade 3	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	17MAY2019 (60)	06JUN2019 (80)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	20MAY2019 (63)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / PYREXIA	15MAY2021 (789)	24MAY2021 (798)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Drug Withdrawn	No
0209-0004	ADIPemPlatinum	Yes	Renal and urinary disorders / Pollakiuria / URINARY FREQUENCY	04OCT2019 (3)	15JAN2020 (106)	Grade 1	Resolved	None	Unrelated / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0004	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	05OCT2019 (4)	28OCT2019 (27)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / INTERMITTENT CONSTIPATION	05OCT2019 (4)	01JAN2020 (92)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Upper-airway cough syndrome / POST NASAL DRIP	06OCT2019 (5)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	07OCT2019 (6)	01DEC2019 (61)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LOWER BACK PAIN.	17OCT2019 (16)	30OCT2019 (29)	Grade 2	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Erythema / FACIAL ERYTHEMA	24OCT2019 (23)	25OCT2019 (24)	Grade 1	Resolved	Medication	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Vascular disorders / Flushing / FACIAL FLUSHING	24OCT2019 (23)	25OCT2019 (24)	Grade 2	Resolved	Medication	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0004	ADIPemPlatinum	Yes	Eye disorders / Eye pain / EYE PAIN	24OCT2019 (23)	24FEB2020 (146)	Grade 1	Resolved	Medication	Unlikely / Probably / Not Applicable / Unlikely	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Gastrointestinal disorders / Oral pain / SORE MOUTH	27OCT2019 (26)	03NOV2019 (33)	Grade 2	Resolved	Other: MOUTH WASH	Unrelated / Definitely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Dysgeusia / TASTE CHANGES	27OCT2019 (26)	01MAR2020 (152)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	27OCT2019 (26)		Grade 2	Ongoing	None	Unrelated / Unlikely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON FACE	03NOV2019 (33)	28NOV2019 (58)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02DEC2019 (62)		Grade 1	Ongoing	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Haemorrhoidal haemorrhage / BLEEDING HAEMORRHOIDS	17DEC2019 (77)	17DEC2019 (77)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed; Dose Reduced	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0004	ADIPemPlatinum	Yes	Infections and infestations / Nasopharyngitis / COLD SYMPTOMS	25JAN2020 (116)	01FEB2020 (123)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Immune system disorders / Anaphylactic reaction / ANAPHYLAXIS	15APR2020 (197)	15APR2020 (197)	Grade 3	Resolved	Withdrawal from Study	Definitely / Not Applicable / Not Applicable / Not Applicable	Drug Withdrawn / Not Applicable / Not Applicable / Not Applicable	No
0209-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	09NOV2019 (5)	11NOV2019 (7)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Psychiatric disorders / Insomnia / INSOMNIA	09NOV2019 (5)	11NOV2019 (7)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / WORSENING RIGHT SIDED CHEST PAIN - NON CARDIAC	09NOV2019 (5)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Gastrointestinal disorders / Mouth ulceration / MOUTH ULCERS	01DEC2019 (27)	08DEC2019 (34)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0209-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / INTERMITTENT FATIGUE	01DEC2019 (27)		Grade 1	Ongoing	None	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	30DEC2019 (56)		Grade 2	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Neutrophil count decreased / LOW NEUTROPHILS	06JAN2020 (63)		Grade 2	Ongoing	Other: BLOODS REPEATED	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0210-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	18JAN2021 (15)		Grade 2	Ongoing	None	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	18JAN2021 (15)		Grade 2	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Injection site reaction / INJECTION SITE REACTION	22JAN2021 (19)		Grade 1	Not Resolved	None	Probably / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0001	PlaceboPemPlatinum	Yes	Vascular disorders / Hot flush / HOT FLASHES	19JUL2019 (3)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	22JUL2019 (6)	24JUL2019 (8)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	22JUL2019 (6)	24JUL2019 (8)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	22JUL2019 (6)	24JUL2019 (8)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	22JUL2019 (6)	18SEP2019 (64)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	10AUG2019 (25)	16AUG2019 (31)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Chest discomfort / CHEST DISCOMFORT & ACHE /RIGHT SIDE PAIN	10AUG2019 (25)	13FEB2020 (212)	Grade 1	Ongoing	None; Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / ACHE RIGHT CHEST, NON-CARDIAC	10AUG2019 (25)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / BACK & RIGHT HIP ACHE	10AUG2019 (25)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Pain in extremity / ACHE IN LEGS (CALVES)	10AUG2019 (25)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	19SEP2019 (65)	26SEP2019 (72)	Grade 2	Resolved with Sequelae	Other: 75% DOSE OF PEMETREXED AND CISPLATIN Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Infections and infestations / Pneumonia / PNEUMONIA	26SEP2019 (72)	27SEP2019 (73)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27SEP2019 (73)	28SEP2019 (74)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	27SEP2019 (73)	28SEP2019 (74)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORT OF BREATH	27SEP2019 (73)	28SEP2019 (74)	Grade 1	Resolved	None	Probably / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	29SEP2019 (75)		Grade 2	Not Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / TENACIOUS SECRETIONS-SPUTUM	30SEP2019 (76)	31OCT2019 (107)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / COUGH/SPUTUM	30SEP2019 (76)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	04OCT2019 (80)		Grade 3	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Renal and urinary disorders / Haematuria / HAEMATURIA	16OCT2019 (92)	20OCT2019 (96)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0001	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Cough / COUGH	01NOV2019 (108)	13FEB2020 (212)	Grade 1	Ongoing	Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RUNNY NOSE	01NOV2019 (108)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Depressed mood / LOW MOOD	01DEC2019 (138)	13FEB2020 (212)	Grade 1	Not Resolved	Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0211-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	09AUG2019 (3)	15AUG2019 (9)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11AUG2019 (5)	13AUG2019 (7)	Grade 1	Resolved with Sequelae	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	11AUG2019 (5)	15AUG2019 (9)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOW APPETITE	11AUG2019 (5)	16AUG2019 (10)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0002	PlaceboPemPlatinum	Yes	Nervous system disorders / Ageusia / NO TASTE TO FOOD	11AUG2019 (5)	23AUG2019 (17)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14AUG2019 (8)	09OCT2019 (64)	Grade 2	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	26AUG2019 (20)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	03SEP2019 (28)	04SEP2019 (29)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Hyperhidrosis / SWEATS	13SEP2019 (38)	14SEP2019 (39)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERING EYES	15SEP2019 (40)	16SEP2019 (41)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RUNNY NOSE	15SEP2019 (40)	16SEP2019 (41)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	26SEP2019 (51)	24OCT2019 (79)	Grade 2	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	10OCT2019 (65)		Grade 3	Ongoing	None	Possibly / Possibly / Possibly / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	10OCT2019 (65)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
0211-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	05OCT2019 (4)	08OCT2019 (7)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	06OCT2019 (5)	20OCT2019 (19)	Grade 1	Resolved	None	Definitely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	10OCT2019 (9)	14OCT2019 (13)	Grade 1	Resolved	None	Definitely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Febrile neutropenia / NEUTROPENIC FEVER	22OCT2019 (21)	23OCT2019 (22)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0003	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	01NOV2019 (31)	24NOV2019 (54)	Grade 1	Resolved	Other: DELAYED A WEEK	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	01NOV2019 (31)	30DEC2019 (90)	Grade 1	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	04NOV2019 (34)	08NOV2019 (38)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	15NOV2019 (45)	28NOV2019 (58)	Grade 4	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Dose Reduced / Dose Reduced / Not Applicable	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	15NOV2019 (45)	28NOV2019 (58)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02DEC2019 (62)	08DEC2019 (68)	Grade 1	Resolved	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	03DEC2019 (63)	06DEC2019 (66)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0003	ADIPemPlatinum	Yes	Infections and infestations / Upper respiratory tract infection / URTI - COLD	16DEC2019 (76)	25DEC2019 (85)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Laceration / CUTS ON FINGERS	17DEC2019 (77)	30DEC2019 (90)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Skin exfoliation / SKIN PEELING ON FINGERS	17DEC2019 (77)	30DEC2019 (90)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	19DEC2019 (79)	22DEC2019 (82)	Grade 1	Resolved with Sequelae	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19DEC2019 (79)	03JAN2020 (94)	Grade 4	Resolved	Other: TREATMENT WITHHELD UNTIL NEUTROPHIL COUNTS IMPROVE	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	19DEC2019 (79)	23JAN2020 (114)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0003	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	30DEC2019 (90)	23JAN2020 (114)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Psychiatric disorders / Insomnia / LACK OF SLEEP	02JAN2020 (93)	20JAN2020 (111)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	04JAN2020 (95)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	04JAN2020 (95)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			Psychiatric disorders / Depressed mood / LOW MOOD	04JAN2020 (95)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	05JAN2020 (96)	11JAN2020 (102)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	23JAN2020 (114)	24APR2020 (206)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0003	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Skin fissures / SKIN SPLITS IN FINGERS AND THUMBS	01FEB2020 (123)	09APR2020 (191)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Skin fissures / SKIN SPLITS ON FINGERS/THUMBS	07FEB2020 (129)	09APR2020 (191)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RED PLAQUE-LIKE RASH - BOTH LEGS	26FEB2020 (148)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Neck pain / NECK PAIN	27FEB2020 (149)	23APR2020 (205)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Neck pain / NECK PAIN	27FEB2020 (149)	30JUL2020 (303)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RED RASH ON LEFT INNER THIGH	03MAR2020 (154)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	21OCT2019 (6)	07NOV2019 (23)	Grade 1	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	08NOV2019 (24)	14NOV2019 (30)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	08NOV2019 (24)	14NOV2019 (30)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Ototoxicity / INTERMITTENT NEUROTOXICITY-HEARING	10NOV2019 (26)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	29NOV2019 (45)	07DEC2019 (53)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	30NOV2019 (46)	09DEC2019 (55)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02DEC2019 (48)	05DEC2019 (51)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0004	PlaceboPemPlatinum	Yes	Eye disorders / Lacrimation increased / WATERING EYES	19DEC2019 (65)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	20DEC2019 (66)	27DEC2019 (73)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20DEC2019 (66)	27DEC2019 (73)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0211-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	02NOV2019 (-4)	09JAN2020 (65)	Grade 1	Ongoing	Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / RT THORAX (CHEST) PAIN NON-CARDIAC	02NOV2019 (-4)	09JAN2020 (65)	Grade 2	Resolved	Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02NOV2019 (-4)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	08NOV2019 (3)	10NOV2019 (5)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / REDUCED APPETITE	13NOV2019 (8)	15NOV2019 (10)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Psychiatric disorders / Restlessness / RESTLESSNESS	13NOV2019 (8)	15NOV2019 (10)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	13NOV2019 (8)	16NOV2019 (11)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLI	17DEC2019 (42)		Grade 3	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Vascular disorders / Deep vein thrombosis / DVT LEFT LOWER LIMB	17DEC2019 (42)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Vascular disorders / Deep vein thrombosis / DVT RIGHT ARM ILIAC VEIN	17DEC2019 (42)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0006	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH OH HIS CHEST	19OCT2020 (6)	25NOV2020 (43)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	07NOV2020 (25)	09NOV2020 (27)	Grade 1	Resolved	None	Possibly / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	09NOV2020 (27)	17DEC2020 (65)	Grade 1	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23NOV2020 (41)	24NOV2020 (42)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	30NOV2020 (48)	02DEC2020 (50)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	07DEC2020 (55)	09DEC2020 (57)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14DEC2020 (62)	16DEC2020 (64)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0006	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	17DEC2020 (65)		Grade 1	Ongoing	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / BREATHLESSNESS	20DEC2020 (68)	20DEC2020 (68)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	20DEC2020 (68)	24DEC2020 (72)	Grade 1	Resolved	None	Unrelated / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / INCREASE SHORT BREATH	21DEC2020 (69)	24DEC2020 (72)	Grade 2	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Corona virus infection / COVID-19	25DEC2020 (73)	02JAN2021 (81)	Grade 5	Fatal	None	Unlikely / Unrelated / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Infections and infestations / Pneumonia / PNEUMONIA	25DEC2020 (73)	02JAN2021 (81)	Grade 5	Fatal	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / WORSENING BREATHLESS	25DEC2020 (73)	02JAN2021 (81)	Grade 5	Fatal	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Not Applicable / Possibly	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Neutropenic sepsis / NEUTROPENIA SEPSIS	25DEC2020 (73)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Respiratory, thoracic and mediastinal disorders / Cough / WORSENING COUGH	25DEC2020 (73)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Not Applicable / Possibly	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	27DEC2020 (75)		Grade 3	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION WITH A RAPID VENTRICULAR RESPONSE	27DEC2020 (75)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Delirium / DELIRIUM	31DEC2020 (79)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0211-0007	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Hyperhidrosis / SWEATS	16DEC2020 (1)	18DEC2020 (3)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0211-0007	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH UPPER CHEST, FOREHEAD AND ARMPIT	29DEC2020 (14)		Grade 2	Ongoing	Medication; Other: REFER TO DERMATOLOGY TEAM	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIC	30DEC2020 (15)	15JAN2021 (31)	Grade 3	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORT OF BREATH	17JAN2021 (33)	02FEB2021 (49)	Grade 1	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			General disorders and administration site conditions / Pyrexia / FEVER: TEMPERATURE OF 39C	07FEB2021 (54)	13FEB2021 (60)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Respiratory, thoracic and mediastinal disorders / Hypoxia / HYPOXIA	07FEB2021 (54)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	07FEB2021 (54)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	17AUG2018 (4)	26AUG2018 (13)	Grade 1	Resolved	Other: CHEMOTHERAPY DEFERRED	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	17AUG2018 (4)	04SEP2018 (22)	Grade 1	Resolved	Other: CHEMOTHERAPY DEFERRED	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	17AUG2018 (4)	11SEP2018 (29)	Grade 2	Resolved with Sequelae	Other: CHEMOTHERAPY DEFERRED	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	17AUG2018 (4)	06NOV2018 (85)	Grade 1	Resolved	Other: CHEMOTHERAPY DEFERRED	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	21AUG2018 (8)	21AUG2018 (8)	Grade 1	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL	22AUG2018 (9)	22AUG2018 (9)	Grade 2	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	22AUG2018 (9)	25SEP2018 (43)	Grade 2	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0001	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / MILD RASH	31AUG2018 (18)	04SEP2018 (22)	Grade 1	Resolved	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	11SEP2018 (29)	30OCT2018 (78)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	23SEP2018 (41)	26SEP2018 (44)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	09OCT2018 (57)	24OCT2018 (72)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH	22OCT2018 (70)	13NOV2018 (92)	Grade 1	Resolved	None	Probably / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	30OCT2018 (78)		Grade 3	Ongoing	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH	19NOV2018 (98)	25FEB2019 (196)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	08OCT2018 (7)	11OCT2018 (10)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / WORSENING LETHARGY	11OCT2018 (10)	13OCT2018 (12)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	11OCT2018 (10)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	20NOV2018 (50)	26NOV2018 (56)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Infections and infestations / Pneumonia / HOSPITAL ACQUIRED PNEUMONIA	23NOV2018 (53)	01DEC2018 (61)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	26NOV2018 (56)		Grade 2	Ongoing	Other: CHEMOTHERAPY CYCLE 4 DISCONTINUED	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0002	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	26DEC2018 (86)		Grade 1	Ongoing	Other: CHEMOTHER APY DISCONTINUED	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	28DEC2018 (88)	31DEC2018 (91)	Grade 1	Resolved	Other: OMITTED C4 CHEMOTHER APY	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Withdrawn / Drug Withdrawn / Not Applicable	No
			Infections and infestations / Pneumonia / RIGHT SIDED PNEUMONIA	05JAN2019 (96)	14JAN2019 (105)	Grade 5	Fatal	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Withdrawn / Not Applicable / Not Applicable / Not Applicable	Yes
0212-0003	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Erythema / ERYTHEMA ON GLUTEAL CLEFT	10OCT2018 (1)	07NOV2018 (29)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Paraesthesia / PARASTHESIA RIGHT LEG	10OCT2018 (1)		Grade 1	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / WORSENING NON CARDIAC CHEST PAIN	14OCT2018 (5)	17OCT2018 (8)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0003	ADIPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Skin ulcer / SKIN ULCERATION	07NOV2018 (29)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / WORSENING NON CARDIAC CHEST PAIN	07DEC2018 (59)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Injury, poisoning and procedural complications / Toxicity to various agents / OPIOID TOXICITY	12DEC2018 (64)	13DEC2018 (65)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Bursitis / OLECRANON BURSTIS	27DEC2018 (79)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0212-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	19JAN2019 (4)		Grade 1	Ongoing	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	03FEB2019 (19)	20MAR2019 (64)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0004	PlaceboPemPlatinum	Yes	Infections and infestations / Sepsis / NON NEUTROPENIC SEPSIS	13FEB2019 (29)	20FEB2019 (36)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Infections and infestations / Infection / NON NEUTROPENIC INFECTION	14FEB2019 (30)	20FEB2019 (36)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Rhinitis / CORYZAL SYMPTOM	28FEB2019 (44)	03MAR2019 (47)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	18MAR2019 (62)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Peripheral swelling / LEG SWELLING	20MAR2019 (64)	17APR2019 (92)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	20MAR2019 (64)		Grade 3	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / SKIN RASH	14APR2019 (89)	17APR2019 (92)	Grade 1	Resolved	None	Probably / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	27MAR2019 (1)		Grade 3	Ongoing	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	30MAR2019 (4)		Grade 2	Ongoing	None	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL CANDIDA	25APR2019 (30)		Grade 1	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Pleural infection / PLEURAL INFECTION	02MAY2019 (37)	08MAY2019 (43)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	30MAY2019 (65)		Grade 2	Resolving	Hospitalization/ Prolonged Hospitalization; Other: 2 UNITS OF RED PACKED CELLS	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	06JUN2019 (72)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0005	PlaceboPemPlatinum	Yes	Infections and infestations / Pleural infection / PLEURAL INFECTION	06JUN2019 (72)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Metabolism and nutrition disorders / Decreased appetite / REDUCED APPETITE	06JUN2019 (72)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
0212-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	20JUL2019 (4)	21JUL2019 (5)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	20JUL2019 (4)	22JUL2019 (6)	Grade 1	Resolved	Medication	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	31JUL2019 (15)	09OCT2019 (85)	Grade 3	Resolved	None	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Lethargy / LETHARGY	01AUG2019 (16)	03AUG2019 (18)	Grade 1	Resolved	None	Probably / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0006	ADIPemPlatinum	Yes	Cardiac disorders / Atrial fibrillation / ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	08AUG2019 (23)	08AUG2019 (23)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	08AUG2019 (23)	23OCT2019 (99)	Grade 1	Resolved	Medication	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	09AUG2019 (24)	11AUG2019 (26)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	21AUG2019 (36)	09DEC2019 (146)	Grade 1	Resolved	Medication	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0212-0007	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	03AUG2019 (6)	06AUG2019 (9)	Grade 1	Resolved	Medication	Possibly / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	03AUG2019 (6)		Grade 1	Ongoing	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0007	ADIPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	03AUG2019 (6)		Grade 2	Ongoing	Medication	Possibly / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Urinary tract infection / RECURRENT URINARY TRACT INFECTION	05AUG2019 (8)		Grade 2	Ongoing	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Urinary tract infection / RECURRENT URINARY TRACT INFECTION	05AUG2019 (8)		Grade 2	Ongoing	Medication	Unlikely / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	08AUG2019 (11)	13AUG2019 (16)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Stomatitis / ORAL MUCOSITIS	08AUG2019 (11)	15AUG2019 (18)	Grade 3	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH	08AUG2019 (11)	15AUG2019 (18)	Grade 1	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Polyuria / POLYURIA	29AUG2019 (32)	09SEP2019 (43)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0007	ADIPemPlatinum	Yes	Nervous system disorders / Dizziness postural / POSTURAL DIZZINESS	13SEP2019 (47)	08NOV2019 (103)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	13SEP2019 (47)		Grade 2	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	14SEP2019 (48)		Grade 2	Ongoing	None	Possibly / Definitely / Not Applicable / Definitely	Dose Not Changed / Drug Withdrawn / Not Applicable / Drug Withdrawn	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	16SEP2019 (50)		Grade 1	Ongoing	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Sensitivity of teeth / SENSITIVE TEETH	11OCT2019 (75)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALAEMIA	14OCT2019 (78)	21OCT2019 (85)	Grade 1	Resolved	Medication	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	15OCT2019 (79)	21OCT2019 (85)	Grade 2	Resolved	Medication	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0007	ADIPemPlatinum	Yes	Eye disorders / Lacrimation increased / WATERY EYES	15OCT2019 (79)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	21OCT2019 (85)		Grade 2	Ongoing	None	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Renal and urinary disorders / Nocturia / NOCTURIA	21OCT2019 (85)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESIA	05NOV2019 (100)		Grade 2	Ongoing	Medication	Unlikely / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	25NOV2019 (120)	02DEC2019 (127)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0212-0008	ADIPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHOEA	10AUG2019 (6)	13AUG2019 (9)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	10AUG2019 (6)		Grade 1	Ongoing	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0008	ADIPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	10AUG2019 (6)		Grade 1	Ongoing	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	30AUG2019 (26)	31AUG2019 (27)	Grade 1	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	09SEP2019 (36)	18SEP2019 (45)	Grade 3	Resolved with Sequelae	Other: BLOOD TRANSFUSION	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	02OCT2019 (59)	07OCT2019 (64)	Grade 3	Resolved	Other: BLOOD TRANSFUSION	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0212-0010	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	23MAR2020 (8)	16APR2020 (32)	Grade 1	Resolved	Medication	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	23MAR2020 (8)	16APR2020 (32)	Grade 2	Resolved	Medication	Unlikely / Definitely / Not Applicable / Definitely	Drug Withdrawn / Drug Withdrawn / Not Applicable / Drug Withdrawn	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	23MAR2020 (8)		Grade 1	Ongoing	Medication	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0011	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	18JUN2020 (3)	20JUN2020 (5)	Grade 2	Resolved	None	Probably /	Dose Not Changed /	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / MACULOPAPULAR RASH	28JUN2020 (13)	15JUL2020 (30)	Grade 1	Resolved	Medication	Possibly /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	16JUL2020 (31)		Grade 2	Ongoing	Medication	Probably /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	16JUL2020 (31)		Grade 2	Ongoing	None	Probably /	Dose Not Changed /	No
			Infections and infestations / Rash pustular / HYPERPIGMENTED PUSTULAR RASH	16JUL2020 (31)		Grade 2	Ongoing	Medication	Possibly /	Drug Interrupted /	No
									Probably /	Drug Interrupted /	
									Not Applicable /	Not Applicable /	
									Probably	Dose Not Changed	
									Unrelated /	Dose Not Changed /	
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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0012	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	16DEC2020 (8)	19DEC2020 (11)	Grade 1	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Infections and infestations / Urinary tract infection / UTI	16DEC2020 (8)	23DEC2020 (15)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood bilirubin increased / RAISED BILIRUBIN	16DEC2020 (8)	24DEC2020 (16)	Grade 2	Resolved	None	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	16DEC2020 (8)		Grade 1	Ongoing	Medication	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			General disorders and administration site conditions / Fatigue / FATIGUE	18DEC2020 (10)	24FEB2021 (78)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Reduced / Not Applicable / Drug Interrupted	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	24DEC2020 (16)	04JAN2021 (27)	Grade 3	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Reduced / Not Applicable / Dose Reduced	No
			Blood and lymphatic system disorders / Lymphopenia / LYMPHOPENIA	18JAN2021 (41)	22FEB2021 (76)	Grade 3	Resolved	None	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0012	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Lymphopenia / LYMPHOPENIA	22FEB2021 (76)	29MAR2021 (111)	Grade 2	Resolved	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	24FEB2021 (78)	01MAR2021 (83)	Grade 2	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANNOREXIA	24FEB2021 (78)		Grade 2	Ongoing	None	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Lethargy / LETHARGY	24FEB2021 (78)		Grade 2	Ongoing	None	Unlikely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	08MAR2021 (90)		Grade 2	Ongoing	Medication	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Weight decreased / WEIGHT LOSS	24MAR2021 (106)		Grade 3	Ongoing	Medication	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Lymphopenia / LYMPHOPENIA	29MAR2021 (111)		Grade 3	Ongoing	Medication	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0212-0012	PlaceboPemPlatinum	Yes	Nervous system disorders / Seizure / SEIZURE	17APR2021 (130)	20APR2021 (133)	Grade 3	Resolved	Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unlikely / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
			Vascular disorders / Orthostatic hypotension / FALL MOST LIKELY DUE TO POSTURAL HYPOTENSION	18APR2021 (131)	18APR2021 (131)	Grade 2	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Lethargy / PROFOUND LETHERGY	03MAY2021 (146)		Grade 3	Ongoing	Other: DEFERRED FOR 1-2 WEEKS	Unlikely / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Missing / Missing / Missing	No
0214-0002	ADIPemPlatinum	Yes	Renal and urinary disorders / Polyuria / FREQUENT DIURESIS	05JUL2021 (6)	08JUL2021 (9)	Grade 1	Resolved	None	Unrelated / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH TO THE FACE AND HEAD	05JUL2021 (6)	31JUL2021 (32)	Grade 2	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER 38.0 C	06JUL2021 (7)	09JUL2021 (10)	Grade 1	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Unknown / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0214-0002	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / INCREASED SOB	07JUL2021 (8)	09JUL2022 (375)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Definitely / Not Applicable	Drug Interrupted / Unknown / Unknown / Not Applicable	Yes
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	08JUL2021 (9)	20JUL2021 (21)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Unknown / Unknown / Not Applicable	Yes
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	08JUL2021 (9)	27JUL2021 (28)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Unknown / Unknown / Not Applicable	Yes
			Investigations / Blood creatinine increased / RAISED CREATININE	08JUL2021 (9)	09JUL2022 (375)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted; Drug Withdrawn / Unknown / Unknown / Not Applicable	Yes
			Gastrointestinal disorders / Mouth ulceration / MOUTH ULCERS	12JUL2021 (13)	27JUL2021 (28)	Grade 2	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Drug Interrupted / Unknown / Unknown / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	14JUL2021 (15)	27JUL2021 (28)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Unknown / Unknown / Unknown / Not Applicable	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / ACID REFLUX	20JUL2021 (21)	09JUL2022 (375)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Unknown / Unknown / Unknown / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0214-0002	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA 0.64 MMOL/L	23JUL2021 (24)	27JUL2021 (28)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
0217-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Abdominal discomfort / ABDOMINAL DISCOMFORT	02AUG2020 (5)	06AUG2020 (9)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / LOOSE STOOLS	02AUG2020 (5)	06AUG2020 (9)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Flatulence / FLACTULANCE EXCESS WIND	02AUG2020 (5)	06AUG2020 (9)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	02AUG2020 (5)	06AUG2020 (9)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	02AUG2020 (5)	06AUG2020 (9)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / LOOSE STOOLS DIARRHOEA	24AUG2020 (27)	24AUG2020 (27)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Abdominal discomfort / SLIGHT ABDOMINAL DISCOMFORT	24AUG2020 (27)	26AUG2020 (29)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	24AUG2020 (27)	26AUG2020 (29)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OD APPETITE	24AUG2020 (27)	26AUG2020 (29)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Alopecia / ALOPECIA	24AUG2020 (27)	24DEC2020 (149)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	25AUG2020 (28)	25AUG2020 (28)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	25AUG2020 (28)	26AUG2020 (29)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	09SEP2020 (43)	16SEP2020 (50)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	21SEP2020 (55)	22SEP2020 (56)	Grade 1	Resolved	Medication	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Abdominal discomfort / ABDOMINAL DISCOMFORT	21SEP2020 (55)	24SEP2020 (58)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Lethargy / LETHARGY	21SEP2020 (55)	24SEP2020 (58)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	07OCT2020 (71)	15OCT2020 (79)	Grade 2	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	19OCT2020 (83)	21OCT2020 (85)	Grade 1	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	19OCT2020 (83)	21OCT2020 (85)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Lethargy / LETHARGY	19OCT2020 (83)	22OCT2020 (86)	Grade 2	Resolved	None	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	22OCT2020 (86)	30OCT2020 (94)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Lethargy / LETHARGY	23OCT2020 (87)	30OCT2020 (94)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	05NOV2020 (100)	13NOV2020 (108)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Lethargy / LETHARGY	05NOV2020 (100)	13NOV2020 (108)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	14NOV2020 (109)	16NOV2020 (111)	Grade 1	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Lethargy / LETHARGY	28NOV2020 (123)	12DEC2020 (137)	Grade 1	Resolved		Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	02DEC2020 (127)	09DEC2020 (134)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Malaise / GENERALLY FEELING UNWELL	12DEC2020 (137)	17DEC2020 (142)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	12DEC2020 (137)	18DEC2020 (143)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	12DEC2020 (137)	24DEC2020 (149)	Grade 1	Resolved		Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	12DEC2020 (137)	24DEC2020 (149)	Grade 2	Resolved with Sequelae	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	24DEC2020 (149)	14JUN2022 (686)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Nervous system disorders / Dizziness / LIGHTHEADEDNESS	28JAN2021 (184)	28JAN2021 (184)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Back pain / RIGHT SIDED BACKACHE	25MAR2021 (240)	10APR2021 (256)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	06APR2021 (252)	14JUN2022 (686)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Hip fracture / FRACTURED LEFT HIP	07JAN2022 (528)	14JUN2022 (686)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Musculoskeletal and connective tissue disorders / Arthralgia / PAIN LEFT HIP	07JAN2022 (528)	14JUN2022 (686)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Blister / SKIN BLISTERS LEFT LOWER LEFT LEG	17JAN2022 (538)	14JUN2022 (686)	Grade 1	Resolved	Other: DRESSINGS TO PROTECT BLISTERS	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	25FEB2022 (577)	15MAR2022 (595)	Grade 1	Resolved with Sequelae	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY TRACT INFECTION	01MAR2022 (581)	09MAR2022 (589)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Missing	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / ANKLE ODEMA	07MAY2021 (3)	09MAY2021 (5)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Lethargy / LETHARGY	07MAY2021 (3)	11MAY2021 (7)	Grade 2	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA -CHANGE OF TASTE	07MAY2021 (3)		Grade 1	Ongoing	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUPS	08MAY2021 (4)	08MAY2021 (4)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Facial paresis / FACIAL WEAKNESS OF BOTH FACE CHEEKS	08MAY2021 (4)	12MAY2021 (8)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / LOOSE STOOLS / DIARRHOEA	11MAY2021 (7)	11MAY2021 (7)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	12MAY2021 (8)	12MAY2021 (8)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0002	PlaceboPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	12MAY2021 (8)		Grade 1	Ongoing	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Skin and subcutaneous tissue disorders / Rash / RED SPOT RASH ON CHEST AND SHOULDERS.	13MAY2021 (9)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Oedema peripheral / ODEMA OF BOTH LOWER LIMBS.	09JUN2021 (36)	20JUN2021 (47)	Grade 1	Resolved	None	Not Applicable / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	09JUN2021 (36)		Grade 1	Ongoing	None	Not Applicable / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Oral herpes / COLD SORE TO THE LOWER LIP	12JUN2021 (39)	22JUN2021 (49)	Grade 1	Resolved	None	Not Applicable / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Eye disorders / Lacrimation increased / WATERY EYES	24JUN2021 (51)	12JUL2021 (69)	Grade 1	Resolved	None	Not Applicable / Probably / Probably / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0217-0002	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Back pain / INTERMITTENT STABBING PAIN IN THE MIDDLE/LOWER BACK, WHICH COMES AND GOES (LASTS A FEW SEC)	21SEP2021 (140)		Grade 2	Ongoing	Other: URINE DIP STICK CHECKED - NAD, ADVISED TO CONTACT GP IF PAIN WILL CONTINUE TO COME	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Eye disorders / Lacrimation increased / WATERY EYES	22SEP2021 (141)		Grade 1	Ongoing	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Skin and subcutaneous tissue disorders / Rash / MILD RASH TO BOTTOMS OF LEGS/ANKLES	23OCT2021 (172)	18NOV2021 (198)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Myalgia / MUSCLE ACHES IN LEFT LOWER LEG	05DEC2021 (215)		Grade 1	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
0218-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	04JUN2020 (4)	23JUN2020 (23)	Grade 2	Resolved	Medication	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	06JUN2020 (6)	10JUN2020 (10)	Grade 2	Resolved	Medication	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Depressed mood / LOW MOOD	06JUN2020 (6)	12JUN2020 (12)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Ear and labyrinth disorders / Hyperacusis / HYPERACUSIS	06JUN2020 (6)	15JUN2020 (15)	Grade 2	Resolved	None	Unrelated / Unlikely / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	06JUN2020 (6)	15JUN2020 (15)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMITING	08JUN2020 (8)	10JUN2020 (10)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	08JUN2020 (8)	12JUN2020 (12)	Grade 2	Resolved	None	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pain / PAIN	11JUN2020 (11)	12OCT2020 (134)	Grade 2	Resolved	None; Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0001	PlaceboPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / INCREASED ALANINE AMINOTRANSFERASE	23JUN2020 (23)	01JUL2020 (31)	Grade 3	Resolved	Medication	Unrelated / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Drug Interrupted / Not Applicable / Dose Reduced; Drug Interrupted	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	23JUN2020 (23)	22SEP2020 (114)	Grade 1	Resolved with Sequelae	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Oral herpes / COLD SORE ON LIP	14JUL2020 (44)	10AUG2020 (71)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	15JUL2020 (45)	06AUG2020 (67)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	10SEP2020 (102)	23SEP2020 (115)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	10SEP2020 (102)	23SEP2020 (115)	Grade 1	Resolved	Other: BLOOD TRANSFUSION GIVEN	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	22SEP2020 (114)		Grade 2	Ongoing	Other: BLOOD TRANSFUSION GIVEN	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	22SEP2020 (114)		Grade 1	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	01OCT2020 (123)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / TASTE ABERATION	01OCT2020 (123)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0218-0002	ADIPemPlatinum	Yes	Uncoded / Uncoded / Missing						Missing / Missing / Missing / Missing	Missing / Missing / Missing / Missing	
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC RIGHT SIDED CHEST PAIN	03JUN2020 (3)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	06JUN2020 (6)		Grade 1	Not Resolved	None	Possibly / Unlikely / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Missing / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON BUTTOCKS	08JUN2020 (8)	15JUN2020 (15)	Grade 1	Resolved	None	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON HANDS	08JUN2020 (8)	15JUN2020 (15)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Missing / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	08JUN2020 (8)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	08JUN2020 (8)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	08JUN2020 (8)		Grade 1	Not Resolved		Unlikely / Unlikely / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Missing / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Sudden death / SUDDEN DEATH ON CHEMOTHERAPY, CAUSE UNKNOWN	18JUN2020 (18)	18JUN2020 (18)	Grade 5	Fatal	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
0218-0003	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / RIB PAIN	07JUL2020 (21)	25AUG2020 (70)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	14JUL2020 (28)	24AUG2020 (69)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	18JUL2020 (32)	21JUL2020 (35)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	20JUL2020 (34)	21JUL2020 (35)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Platelet count increased / PLATELET COUNT INCREASED	03AUG2020 (48)	11AUG2020 (56)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0003	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / RIB PAIN	25AUG2020 (70)	02SEP2020 (78)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / RIB PAIN	02SEP2020 (78)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	15SEP2020 (91)	16NOV2020 (153)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	15SEP2020 (91)	17NOV2020 (154)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	10NOV2020 (147)	16NOV2020 (153)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	24NOV2020 (161)	30NOV2020 (167)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0003	ADIPemPlatinum	Yes	Investigations / Blood iron decreased / REDUCED IRON LEVELS	24NOV2020 (161)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / LOWER RESPIRATORY TRACT INFECTION	01DEC2020 (168)	15DEC2020 (182)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	01DEC2020 (168)		Grade 2	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Corona virus infection / ASYMPTOMATIC COVID + TEST	31JAN2021 (229)	10FEB2021 (239)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	18MAY2021 (336)	24MAY2021 (342)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
0218-0005	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / RIB PAIN	25JUN2020 (-4)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	29JUN2020 (1)	13JUL2020 (15)	Grade 1	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	30JUN2020 (2)	30JUN2020 (2)	Grade 1	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	30JUN2020 (2)		Grade 2	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	04JUL2020 (6)		Grade 1	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	13JUL2020 (15)		Grade 2	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Injection site reaction / INJECTION SITE REACTION	15JUL2020 (17)	28JUL2020 (30)	Grade 2	Resolved	Medication	Probably / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON LEGS	15JUL2020 (17)	28JUL2020 (30)	Grade 2	Resolved	Medication	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0005	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Arthralgia / JOINT PAINS	16JUL2020 (18)	04AUG2020 (37)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	18JUL2020 (20)	24JUL2020 (26)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Neutropenic sepsis / NEUTROPENIC SEPSIS	18JUL2020 (20)	24JUL2020 (26)	Grade 3	Resolved	Medication; Hospitalization; Prolonged Hospitalization	Possibly / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Reduced; Drug Interrupted / Not Applicable / Dose Reduced; Drug Interrupted	Yes
			Skin and subcutaneous tissue disorders / Rash / RASH ON BODY	18JUL2020 (20)	28JUL2020 (30)	Grade 2	Resolved	Medication	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY EMBOLISM	22SEP2020 (86)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	28SEP2020 (92)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0005	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	01OCT2020 (95)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	08OCT2020 (102)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Thermal burn / BURN RIGHT UPPER ARM	19OCT2020 (113)		Grade 2	Resolving	Other: DRESSING APPLIED	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	20OCT2020 (114)	24OCT2020 (118)	Grade 2	Resolved	Other: BLOOD TRANSFUSION, 2 UNITS	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	20OCT2020 (114)	29OCT2020 (123)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	29OCT2020 (123)	03NOV2020 (128)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0006	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	21JUL2020 (8)	22JUL2020 (9)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed; Drug Interrupted / Dose Reduced / Not Applicable / Dose Reduced	No
			Gastrointestinal disorders / Diarrhoea / DIAHRROEA	21JUL2020 (8)	23JUL2020 (10)	Grade 2	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Reduced / Not Applicable / Dose Reduced	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	21JUL2020 (8)	24JUL2020 (11)	Grade 1	Resolved	None	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Paraesthesia / TINGLING TOES	21JUL2020 (8)	28JUL2020 (15)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Vulvovaginal candidiasis / VAGINAL THRUSH	28JUL2020 (15)	04AUG2020 (22)	Grade 2	Resolved	Medication	Unrelated / Unlikely / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Lacrimation increased / WATERY EYES	28JUL2020 (15)	08AUG2020 (26)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Rhinitis allergic / ALLERGIC RHINITIS	28JUL2020 (15)	08AUG2020 (26)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0006	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dry mouth / DRY MOUTH	30JUL2020 (17)	06AUG2020 (24)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0218-0007	PlaceboPemPlatinum	Yes	Investigations / Liver function test abnormal / DERANGED LIVER FUNCTION	20JUL2020 (1)		Grade 3	Ongoing	None	Possibly / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Reduced / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Oedema peripheral / ANKLE OEDEMA	26JUL2020 (7)	11AUG2020 (23)	Grade 1	Resolved	Other: DEXAMETHA SONE DOSE REDUCED	Unrelated / Not Applicable / Unrelated	Dose Not Changed / Not Applicable / Missing / Not Applicable	No
			Gastrointestinal disorders / Abdominal distension / BLOATED SENSATION	27JUL2020 (8)	31JUL2020 (12)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / RASH - RIGHT HAND	27JUL2020 (8)	31JUL2020 (12)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	03AUG2020 (15)	05AUG2020 (17)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Possibly / Possibly / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Oedema peripheral / ANKLE OEDEMA	14AUG2020 (26)	27AUG2020 (39)	Grade 1	Resolved	Medication	Unlikely / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0007	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	14AUG2020 (26)	22SEP2020 (65)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	14AUG2020 (26)	22SEP2020 (65)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood alkaline phosphatase increased / RAISED ALKALINE PHOSPHATASE	20AUG2020 (32)		Grade 3	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	27AUG2020 (39)	30AUG2020 (42)	Grade 2	Resolved	Other: BLOOD TRANSFUSION	Possibly / Possibly / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / TASTE ABERRATION	27AUG2020 (39)		Grade 1	Ongoing	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	30AUG2020 (42)	01OCT2020 (74)	Grade 1	Resolved with Sequelae	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	10SEP2020 (53)	17SEP2020 (60)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0007	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	10SEP2020 (53)		Grade 1	Ongoing	None	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Missing / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Dry skin / DRY SKIN	17SEP2020 (60)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	22SEP2020 (65)		Grade 1	Ongoing	Other: SUPPLEMENTARY DRINKS	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	22SEP2020 (65)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Missing / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	28SEP2020 (71)	08OCT2020 (81)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	29SEP2020 (72)	08OCT2020 (81)	Grade 2	Resolved with Sequelae	None	Unrelated / Missing / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	01OCT2020 (74)		Grade 2	Ongoing		Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0007	PlaceboPemPlatinum	Yes	Infections and infestations / Oral candidiasis / ORAL THRUSH	01OCT2020 (74)		Grade 2	Ongoing	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed; Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed; Drug Interrupted	No
			Injury, poisoning and procedural complications / Muscle strain / RIGHT GROIN STRAIN	06OCT2020 (79)		Grade 1	Unknown		Unrelated / Unrelated / Not Applicable / Unrelated	Missing / Missing / Missing / Missing	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / DYSPNOEA ON EXERTION	08OCT2020 (81)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0218-0008	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	11AUG2020 (8)	17AUG2020 (14)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH	18AUG2020 (15)	28AUG2020 (25)	Grade 1	Resolved	Medication	Unrelated / Definitely / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Extrasystoles / CARDIAC RHYTHM CHANGE- BIGEMINY	27AUG2020 (24)		Grade 2	Not Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0008	PlaceboPemPlatinum	Yes	Injury, poisoning and procedural complications / Contusion / BRUSIE TO RIGHT FOREARM	19NOV2020 (108)	17DEC2020 (136)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0218-0012	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	26SEP2020 (6)	03OCT2020 (13)	Grade 1	Resolved	None	Possibly / Possibly / Unrelated /	Dose Not Changed / Dose Not Changed / Not Applicable /	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	27SEP2020 (7)	02OCT2020 (12)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	27SEP2020 (7)	02OCT2020 (12)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27SEP2020 (7)		Grade 2	Ongoing	None	Possibly / Probably / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / TASTE ABBERRATION	27SEP2020 (7)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / NOSE BLEEDS	03OCT2020 (13)	04OCT2020 (14)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Reduced	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0012	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	05OCT2020 (15)	08OCT2020 (18)	Grade 2	Resolved	None	Possibly / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Reduced	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	05OCT2020 (15)	08OCT2020 (18)	Grade 2	Resolved	None	Possibly / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Reduced	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / SHORTNESS OF BREATH ON EXERTION	05OCT2020 (15)		Grade 2	Ongoing	None	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Neutropenic sepsis / NEUTROPENIC SEPSIS	26OCT2020 (36)	28OCT2020 (38)	Grade 4	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Drug Interrupted / Not Applicable / Dose Reduced	Yes
0218-0013	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION	29SEP2020 (1)	06OCT2020 (8)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / LOCALISED RASH RIGHT BUTTOCK	19OCT2020 (21)		Grade 1	Ongoing	None	Probably / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0014	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / INDIGESTION	27OCT2020 (8)	10NOV2020 (22)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27OCT2020 (8)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON FEET AND ANKLES	11NOV2020 (23)	19NOV2020 (31)	Grade 1	Resolved	Medication	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Laceration / CUT ON HEAD	01DEC2020 (43)	10DEC2020 (52)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RUNNY NOSE	01DEC2020 (43)	09MAR2021 (141)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON BODY	03DEC2020 (45)		Grade 2	Resolving	Medication	Probably / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	07JAN2021 (80)	12FEB2021 (116)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0014	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	07JAN2021 (80)	01MAR2021 (133)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	07JAN2021 (80)	09MAR2021 (141)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	07JAN2021 (80)	09MAR2021 (141)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Back pain / BACK PAIN	02MAR2021 (134)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	01APR2021 (164)	01APR2021 (164)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Gait disturbance / DIFFICULTY WALKING	10APR2021 (173)		Grade 2	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / RIGHT HIP PAIN	10APR2021 (173)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0015	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	23JAN2021 (5)		Grade 2	Ongoing	Medication	Unrelated /	Dose Not Changed /	No
			Investigations / Weight decreased / WEIGHT LOSS	26JAN2021 (8)	02FEB2021 (15)	Grade 2	Resolved with Sequelae	Medication	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Dysphagia / DYSPHAGIA	02FEB2021 (15)		Grade 1	Ongoing	Medication	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	09FEB2021 (22)		Grade 2	Ongoing	Medication	Unrelated /	Dose Not Changed /	No
			Infections and infestations / Corona virus infection / COVID INFECTION	19FEB2021 (32)		Grade 2	Ongoing	None	Unrelated /	Drug Interrupted /	No
									Unrelated /	Dose Not Changed /	
0218-0016	ADIPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / LOOSE STOOLS	08MAR2021 (7)	09MAR2021 (8)	Grade 1	Resolved	None	Possibly /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	08MAR2021 (7)	09MAR2021 (8)	Grade 2	Resolved	Medication	Possibly /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0016	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	08MAR2021 (7)	16MAR2021 (15)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMITING	09MAR2021 (8)	09MAR2021 (8)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Mouth ulceration / MOUTH ULCERS	11MAR2021 (10)	06APR2021 (36)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash / RASH ON CHEST	27JUL2021 (148)	17AUG2021 (169)	Grade 1	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Myocardial infarction / MYOCARDIUM INFARCTION	05NOV2021 (249)	18NOV2021 (262)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0218-0018	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / DECREASED APETITE	04APR2021 (6)	20APR2021 (22)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	04APR2021 (6)	29APR2021 (31)	Grade 2	Resolved	Medication	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0018	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	04APR2021 (6)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Fluid intake reduced / DECREASED FLUID INTAKE	04APR2021 (6)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Somnolence / SOMNOLENCE	06APR2021 (8)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Sepsis / NON NEUTROPENIC SEPSIS	08APR2021 (10)	15APR2021 (17)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Reduced	Yes
			General disorders and administration site conditions / Pyrexia / PYREXIA	27APR2021 (29)	29APR2021 (31)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	27APR2021 (29)	29APR2021 (31)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	27APR2021 (29)	29APR2021 (31)	Grade 2	Resolved	Medication	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0018	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dysphagia / DIFFICULTY SWALLOWING	27APR2021 (29)	06MAY2021 (38)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	27APR2021 (29)	06MAY2021 (38)	Grade 2	Resolved	Medication	Possibly / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	27APR2021 (29)	10MAY2021 (42)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	29APR2021 (31)	06MAY2021 (38)	Grade 1	Resolved	Medication	Unlikely / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Oral pain / SORE MOUTH	29APR2021 (31)	11MAY2021 (43)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	29APR2021 (31)	11MAY2021 (43)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	29APR2021 (31)	11MAY2021 (43)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0018	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	29APR2021 (31)	11MAY2021 (43)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	06MAY2021 (38)	11MAY2021 (43)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	11MAY2021 (43)	27MAY2021 (59)	Grade 1	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11MAY2021 (43)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Decubitus ulcer / PRESSURE SORE ON SACRUM	11MAY2021 (43)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Productive cough / PRODUCTIVE COUGH	25MAY2021 (57)	31MAY2021 (63)	Grade 2	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Dry eye / DRY EYE RIGHT EYE	03JUN2021 (66)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0018	ADIPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	08JUN2021 (71)	09JUN2021 (72)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0218-0019	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	20APR2021 (1)	04MAY2021 (15)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	24APR2021 (5)	04MAY2021 (15)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Flatulence / FLATULENCE	28APR2021 (9)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11MAY2021 (22)	27MAY2021 (38)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	20MAY2021 (31)	27MAY2021 (38)	Grade 1	Resolved	Medication	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Dry eye / DRY EYE	20MAY2021 (31)		Grade 1	Ongoing	Medication	Unlikely / Possibly / Unrelated / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0218-0019	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	03JUN2021 (45)	30JUN2021 (72)	Grade 1	Resolved	None	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	03JUN2021 (45)	13JUL2021 (85)	Grade 1	Resolved	Medication	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / DECREASED APPETITE	10JUN2021 (52)		Grade 1	Ongoing	None	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01JUL2021 (73)		Grade 2	Ongoing	None	Possibly / Possibly / Unrelated / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANAEMIA	08JUL2021 (80)	14JUL2021 (86)	Grade 1	Resolved	Other: BLOOD TRASNFIUSION	Unrelated / Possibly / Not Applicable / Possibly	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
0219-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	11NOV2020 (1)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pain / PAIN	18NOV2020 (8)	23DEC2020 (43)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / INCREASED FATIGUE	30NOV2020 (20)	30NOV2020 (20)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	30NOV2020 (20)	07DEC2020 (27)	Grade 4	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable / Dose Reduced; Drug Interrupted	No
			General disorders and administration site conditions / Fatigue / FATIGUE	30NOV2020 (20)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	30NOV2020 (20)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	16DEC2020 (36)	17DEC2020 (37)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0219-0002	ADIPemPlatinum	Yes	Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	11JAN2021 (6)	31JAN2021 (26)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Chills / CHILLS	12JAN2021 (7)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	23JAN2021 (18)	25JAN2021 (20)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Renal and urinary disorders / Dysuria / DYSURIA	23JAN2021 (18)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	01FEB2021 (27)	10FEB2021 (36)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Not Applicable / Unlikely	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	Yes
			Psychiatric disorders / Insomnia / INSOMNIA	02FEB2021 (28)	02FEB2021 (28)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	24FEB2021 (50)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Lung infection / LUNG INFECTION	27MAR2021 (81)	08APR2021 (93)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Not Applicable / Unlikely	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0003	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Flatulence / FLATULENCE	20JAN2021 (1)		Grade 1	Ongoing	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	27JAN2021 (8)	08FEB2021 (20)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASE	08FEB2021 (20)	14FEB2021 (26)	Grade 2	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			General disorders and administration site conditions / Fatigue / FATIGUE	08FEB2021 (20)	15FEB2021 (27)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Eye disorders / Dry eye / DRY EYE	08FEB2021 (20)	26APR2021 (97)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	08FEB2021 (20)	09JUN2021 (141)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASE	15FEB2021 (27)	24FEB2021 (36)	Grade 1	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0003	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Oedema peripheral / EDEMA LIMBS	15FEB2021 (27)	29MAR2021 (69)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	15FEB2021 (27)	09JUN2021 (141)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	15FEB2021 (27)		Grade 1	Ongoing	None	Unlikely / Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMITING	24FEB2021 (36)	29MAR2021 (69)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTAXIS	25FEB2021 (37)	09JUN2021 (141)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / THROMBOEMBOLIC EVENT - PULMONARY EMBOLISM	03MAR2021 (43)		Grade 3	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	29MAR2021 (69)	05APR2021 (76)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0003	PlaceboPemPlatinum	Yes	Eye disorders / Lacrimation increased / WATERING EYES	29MAR2021 (69)	09JUN2021 (141)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Reproductive system and breast disorders / Prostatism / PROSTATISM	29MAR2021 (69)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	26APR2021 (97)	09JUN2021 (141)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR	26APR2021 (97)	09JUN2021 (141)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	17MAY2021 (118)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0219-0004	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	25JAN2021 (6)	28FEB2021 (40)	Grade 2	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Gastrointestinal pain / GASTROINTESTINAL PAIN	27JAN2021 (8)	28JAN2021 (9)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0004	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR (BOTH ARMS)	03FEB2021 (15)	29MAR2021 (69)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Vascular disorders / Hot flush / HOT FLASHES	24FEB2021 (36)	22MAR2021 (62)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01MAR2021 (41)	11APR2021 (82)	Grade 1	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	22MAR2021 (62)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Vascular disorders / Hypertension / HYPERTENSION	24MAR2021 (64)		Grade 3	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12APR2021 (83)	04MAY2021 (105)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	26APR2021 (97)	05MAY2021 (106)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dry mouth / DRY MOUTH	26APR2021 (97)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / CHEST AND RIGHT SHOULDER PAIN (NON-CARDIAC)	01MAY2021 (102)	04MAY2021 (105)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Fall / FALL	04MAY2021 (105)	05MAY2021 (106)	Grade 1	Resolved	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	05MAY2021 (106)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / CHEST AND RIGHT SHOULDER PAIN (NON-CARDIAC)	10MAY2021 (111)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	24MAY2021 (125)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0004	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEOA	24MAY2021 (125)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0219-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	31MAR2021 (8)	05MAY2021 (43)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / INTERMITTENT EPISTAXIS	02APR2021 (10)	24MAY2021 (62)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Muscle spasms / INTERMITTENT CRAMP (CALF)	08APR2021 (16)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / INTERMITTENT CONSTIPATION	11APR2021 (19)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECEASE	12APR2021 (20)	28APR2021 (36)	Grade 4	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Dose Reduced; Drug Interrupted / Not Applicable / Dose Reduced; Drug Interrupted	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0005	ADIPemPlatinum	Yes	Eye disorders / Photophobia / PHOTOPHOBIA	12APR2021 (20)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS	16APR2021 (24)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / PLEURITIC PAIN (LEFT SIDE)	19APR2021 (27)	24MAY2021 (62)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	23APR2021 (31)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Renal and urinary disorders / Urinary incontinence / URINARY INCONTINENCE	23APR2021 (31)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	25APR2021 (33)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Peripheral sensory neuropathy / PERIPHERAL SENSORY NEUROPATHY	26APR2021 (34)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	06MAY2021 (44)	07MAY2021 (45)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Paronychia / PARONYCHIA	07MAY2021 (45)	12JUL2021 (111)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASE	10MAY2021 (48)	24MAY2021 (62)	Grade 3	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Gastrointestinal disorders / Stomatitis / MUCOSITIS ORAL	13MAY2021 (51)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Rash maculo-papular / RASH MACULO-PAPULAR (LEGS AND BACK)	13MAY2021 (51)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	24MAY2021 (62)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	27MAY2021 (65)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0005	ADIPemPlatinum	Yes	Nervous system disorders / Memory impairment / MEMORY IMPAIRMENT (LOSS)	27MAY2021 (65)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Skin and subcutaneous tissue disorders / Photosensitivity reaction / PHOTSENSITIVITY	03JUN2021 (72)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dysphonia / VOICE ALTERATION (CROAKY)	04JUN2021 (73)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Inguinal hernia / WORSENING LEFT INGUINAL HERNIA	14JUN2021 (83)		Grade 2	Ongoing	Other: PATIENT FITTED WITH HERNIA TRUSS	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			General disorders and administration site conditions / Fatigue / FATIGUE	18JUN2021 (87)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	18JUN2021 (87)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	23JUL2021 (122)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Infections and infestations / Corona virus infection / COVID-19	30JUL2021 (129)		Grade 3	Ongoing	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
0219-0006	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dry mouth / DRY MOUTH	23APR2021 (3)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Muscle spasms / MUSCLE CRAMP	26APR2021 (6)	05MAY2021 (15)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	26APR2021 (6)	06MAY2021 (16)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	03MAY2021 (13)	06MAY2021 (16)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	05MAY2021 (15)		Grade 1	Ongoing	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0219-0006	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal pain / RIGHT SHOULDER PAIN	15MAY2021 (25)	20MAY2021 (30)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01JUN2021 (42)		Grade 1	Ongoing	None	Unlikely / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / INTERMITTENT DYSGEUSIA	06JUN2021 (47)		Grade 1	Ongoing	None	Unrelated / Possibly / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC CHEST PAIN	07JUN2021 (48)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0301-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	08JAN2019 (23)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0301-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	18DEC2018 (2)	20DEC2018 (4)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0301-0002	PlaceboPemPlatinum	Yes	Skin and subcutaneous tissue disorders / Rash / RASH TO GROIN REGION	28DEC2018 (12)	20JUN2019 (186)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuralgia / NEUROPATHIC PAIN	02MAR2019 (76)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Ear and labyrinth disorders / Tinnitus / TINNITUS	13MAR2019 (87)	23APR2019 (128)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Injury, poisoning and procedural complications / Infusion related reaction / INFUSION SKIN REACTION- PRURITIS AND ERYTHEMA TO TRUNK AND NECK	03APR2019 (108)	03APR2019 (108)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Interrupted / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / DRY COUGH	22JUN2019 (188)		Grade 1	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0301-0004	PlaceboPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	15MAR2019 (4)	18MAR2019 (7)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0301-0004	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal stiffness / BACK STIFFNESS	26MAR2019 (15)	08JUL2020 (485)	Grade 1	Unknown	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
0301-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	04JUL2019 (3)	05JUL2019 (4)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	Yes
			Skin and subcutaneous tissue disorders / Rash / SKIN RASH	05JUL2019 (4)	12JUL2020 (377)	Grade 1	Unknown	Medication	Unrelated / Probably / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERY EYES	14AUG2019 (44)	10SEP2019 (71)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Eye disorders / Lacrimation increased / WATERY EYES	19SEP2019 (80)	05NOV2019 (127)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	01NOV2019 (123)	15DEC2019 (167)	Grade 1	Resolved	None	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	01NOV2019 (123)	15DEC2019 (167)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0301-0006	PlaceboPemPlatinum	Yes	Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	24SEP2019 (64)	13NOV2019 (114)	Grade 2	Resolved	Other: DOSE REDUCTION	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Missing	No
			Skin and subcutaneous tissue disorders / Swelling face / FACIAL SWELLING	28OCT2019 (98)	20DEC2020 (517)	Grade 1	Unknown	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERY EYES	03NOV2019 (104)	10DEC2019 (141)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / FACIAL RASH	03NOV2019 (104)	10DEC2019 (141)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	14NOV2019 (115)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APPETITE	20FEB2020 (213)		Grade 1	Ongoing	None	Possibly / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain upper / RIGHT UPPER ABDOMEN AND CHEST PAIN	22FEB2020 (215)	25FEB2020 (218)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0301-0007	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal pain upper / EPIGASTRIC ABDOMINAL PAIN	22OCT2019 (8)	30OCT2019 (16)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Constipation / CONSTIPATION	22OCT2019 (8)	30OCT2019 (16)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	09NOV2019 (26)	11NOV2019 (28)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	17DEC2019 (64)	01FEB2020 (110)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNOEA	17DEC2019 (64)	01JUN2020 (231)	Grade 1	Unknown	None	Unrelated / Unrelated / Unrelated / Not Applicable	Unknown / Not Applicable / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / WATERY EYES	03JAN2020 (81)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Dizziness postural / POSTURAL DIZZINESS	03JAN2020 (81)		Grade 1	Ongoing	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0301-0007	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	18FEB2020 (127)	18FEB2020 (127)	Grade 1	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed; Unknown / Dose Not Changed / Dose Not Changed / Not Applicable	No
0302-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	27JAN2020 (6)	24MAR2020 (63)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	28JAN2020 (7)	28JAN2020 (7)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Hypoaesthesia / LOCAL NUMBNESS TO L HIP	30JAN2020 (9)	24MAR2020 (63)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Upper respiratory tract infection / UPPER RESPIRATORY TRACT INFECTION	07FEB2020 (17)	24FEB2020 (34)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	16FEB2020 (26)	24FEB2020 (34)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0302-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	16FEB2020 (26)		Grade 1	Ongoing	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	03MAR2020 (42)	25MAY2020 (125)	Grade 2	Resolved with Sequelae	Other: SWITCHED TO CARBOPLATIN WITH MEDICAL MONITOR APPROVAL	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Missing	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	26MAY2020 (126)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Definitely / Unrelated	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Dose Not Changed	No
0303-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	05MAR2020 (3)	06MAR2020 (4)	Grade 1	Resolved	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	06MAR2020 (4)	10MAR2020 (8)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	10MAR2020 (8)	14MAR2020 (12)	Grade 2	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0303-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Secretion discharge / MUCOUS	17MAR2020 (15)		Grade 2	Ongoing	None	Unlikely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	23MAR2020 (21)	30MAR2020 (28)	Grade 4	Resolved	Other: DELAYED 1 WEEK	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	20APR2020 (49)	27APR2020 (56)	Grade 3	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	03MAY2020 (62)	06MAY2020 (65)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Immune system disorders / Seasonal allergy / HAY FEVER	16MAY2020 (75)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	18MAY2020 (77)		Grade 3	Resolving	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	26MAY2020 (85)		Grade 2	Ongoing	None	Unlikely / Unrelated / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0303-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Peripheral swelling / LEFT HAND SWELLING	10JUN2020 (100)	08SEP2020 (190)	Grade 1	Resolved	Other: JUST A NOTE- THE DOCTOR HAS RECORDED THIS EVENT AS UNLIKELY RELATED TO STUDY DRUGS, BUT HAS ALSO ADDED THAT IT IS AN UNKNOWN ETIOLOGY BUT UNLIKELY RELATED TO TREATMENT	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Infections and infestations / Lung infection / LUNG INFECTION	19AUG2020 (170)	27AUG2020 (178)	Grade 3	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization	Possibly / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes
			Respiratory, thoracic and mediastinal disorders / Dysphonia / HOARSE VOICE	08SEP2020 (190)		Grade 2	Ongoing	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0303-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	15SEP2020 (197)		Grade 2	Not Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			General disorders and administration site conditions / Non-cardiac chest pain / CHEST PAIN (NON CARDIAC)	19OCT2020 (231)	20OCT2020 (232)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Pneumonia / PNEUMONIA	09NOV2020 (252)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
0303-0002	ADIPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Joint swelling / ANKLE SWELLING	01AUG2020 (4)	20AUG2020 (23)	Grade 1	Resolved	None	Unlikely / Unlikely / Possibly / Missing	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Cognitive disorder / COGNITIVE CHANGES	01AUG2020 (4)	20AUG2020 (23)	Grade 1	Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Unknown	No
			General disorders and administration site conditions / Chest discomfort / CHEST TIGHTNESS	01AUG2020 (4)		Grade 1	Not Resolved	None	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0303-0002	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19AUG2020 (22)	26AUG2020 (29)	Grade 4	Resolved	None	Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Reduced; Drug Interrupted / Dose Reduced; Drug Interrupted / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	21AUG2020 (24)	01SEP2020 (35)	Grade 1	Resolved with Sequelae	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	02SEP2020 (36)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Fall / FALL/ COLLAPSE	03SEP2020 (37)	05SEP2020 (39)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Drug Interrupted; Drug Withdrawn / Dose Not Changed / Dose Not Changed / Missing	Yes
0304-0001	PlaceboPemPlatinum	Yes	Cardiac disorders / Angina pectoris / CARDIAC CHEST PAIN	08JUN2018 (4)	08JUN2018 (4)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0001	PlaceboPemPlatinum	Yes	Cardiac disorders / Myocardial infarction / MYOCARDIAL INFARCTION	08JUN2018 (4)	08JUN2018 (4)	Grade 4	Resolved	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	08JUN2018 (4)	12JUN2018 (8)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	08JUN2018 (4)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Vascular disorders / Hypotension / HYPOTENSION	10JUN2018 (6)	10JUN2018 (6)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Troponin increased / TROPONIN INCREASED	10JUN2018 (6)		Grade 3	Unknown	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	15JUN2018 (11)	28JUN2018 (24)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0001	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	20JUN2018 (16)	20JUN2018 (16)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Cerebrovascular accident / LEFT MIDDLE CEREBRAL ARTERY (MCA) STROKE	20JUN2018 (16)	04JUL2018 (30)	Grade 4	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Eye disorders / Ocular hyperaemia / LEFT EYE REDNESS	03JUL2018 (29)	04JUL2018 (30)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Nervous system disorders / Cerebrovascular accident / LEFT MIDDLE CEREBRAL ARTERY (MCA) STROKE	05JUL2018 (31)	12JUL2018 (38)	Grade 2	Ongoing	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0304-0002	ADIPemPlatinum	Yes	Nervous system disorders / Lethargy / LETHARGY	08FEB2020 (4)	11FEB2020 (7)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Musculoskeletal and connective tissue disorders / Flank pain / WORSE L FLANK PAIN	08FEB2020 (4)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / ACUTE CONSTIPATION	28FEB2020 (24)	04MAR2020 (29)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0002	ADIPemPlatinum	Yes	Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	03MAR2020 (28)	05MAR2020 (30)	Grade 2	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	03MAR2020 (28)		Grade 2	Resolving	Medication	Unlikely / Unlikely / Unlikely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			General disorders and administration site conditions / Sudden death / SUDDEN DEATH	08MAR2020 (33)	08MAR2020 (33)	Grade 5	Fatal	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
0304-0003	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	30JUN2020 (36)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal discomfort / GASTROINTESTINAL DISORDERS, OTHER (DISCOMFORT)	05AUG2020 (72)	05AUG2020 (72)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Cough / DRY COUGH	09FEB2021 (260)	12FEB2021 (263)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0003	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	11FEB2021 (262)	12FEB2021 (263)	Grade 1	Resolved	Surgical/ Diagnostic Procedure	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Infections and infestations / Candida infection / THRUSH	11FEB2021 (262)	16FEB2021 (267)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Pleuritic pain / MILD PLEURITIC PAIN	04MAR2021 (283)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0304-0004	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	08JUL2020 (9)		Grade 2	Ongoing	Other: ORAL NUTRITIONAL SUPPLEMENT S	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20JUL2020 (21)		Grade 1	Ongoing	None	Probably / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DYSGEUSIA	20JUL2020 (21)		Grade 1	Ongoing	None	Possibly / Possibly / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA (INTERMITTENT)	27JUL2020 (28)		Grade 1	Ongoing	Medication	Possibly / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Weight decreased / WEIGHT LOSS	30JUL2020 (31)	12AUG2020 (44)	Grade 1	Resolved	None	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	08AUG2020 (40)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Investigations / Weight decreased / WEIGHT LOSS	12AUG2020 (44)		Grade 2	Ongoing	Other: DIETITION REFERRAL + CONSULTATION	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	31AUG2020 (63)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Injury, poisoning and procedural complications / Procedural pain / R) THORAX PAIN (POST DRAIN REMOVAL)	02SEP2020 (65)		Grade 2	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0304-0004	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	15SEP2020 (78)		Grade 3	Ongoing	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pleural effusion / PLEURAL EFFUSION	16SEP2020 (79)	23SEP2020 (86)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes
0305-0001	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / THORACIC PAIN - NON CARDIAC (RIGHT LOWER CHEST)	30JUL2018 (1)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	05AUG2018 (7)		Grade 1	Ongoing	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	05AUG2018 (7)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Immune system disorders / Hypersensitivity / ALLERGIC REACTION TO UNKNOWN SOURCE	08AUG2018 (10)	08AUG2018 (10)	Grade 2	Resolved	Medication	Unlikely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0001	ADIPemPlatinum	Yes	Psychiatric disorders / Insomnia / INSOMNIA	08AUG2018 (10)	27AUG2018 (29)	Grade 2	Resolved	Medication	Probably / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Oral candidiasis / ORAL THRUSH	08AUG2018 (10)		Grade 2	Unknown	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed; Unknown / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Febrile neutropenia / FEBRILE NEUTROPENIA	17AUG2018 (19)	19AUG2018 (21)	Grade 4	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESAEMIA	17AUG2018 (19)	19AUG2018 (21)	Grade 2	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Febrile neutropenia / FEBRILE NEUTROPENIA	19AUG2018 (21)	20AUG2018 (22)	Grade 3	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperglycaemia / HYPERGLYCEMIA	21AUG2018 (23)	23AUG2018 (25)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Blood and lymphatic system disorders / Neutropenia / MILD NEUTROPENIA	10SEP2018 (43)	12SEP2018 (45)	Grade 1	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / MILD ANAEMIA	10SEP2018 (43)		Grade 1	Ongoing	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESAEMIA	17SEP2018 (50)	18SEP2018 (51)	Grade 3	Resolved	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	18SEP2018 (51)	20SEP2018 (53)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			General disorders and administration site conditions / Injection site pain / SORE LEFT THIGH AT INJECTION SITE	18SEP2018 (51)	21SEP2018 (54)	Grade 1	Resolved	None	Definitely / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Gastrooesophageal reflux disease / GASTRO OESOPHAGEAL REFLUX	18SEP2018 (51)		Grade 2	Ongoing	Medication	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / LRTI (RESPIRATORY INFECTION)	22OCT2018 (85)	04NOV2018 (98)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / SHORTNESS OF BREATH	27OCT2018 (90)	28OCT2018 (91)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	29OCT2018 (92)		Grade 2	Ongoing	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / LOWER RESPIRATORY TRACK INFECTION	17NOV2018 (111)	23NOV2018 (117)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Weight decreased / WEIGHT LOSS	03DEC2018 (127)		Grade 1	Not Resolved	Other: REFERRED TO DIETITIAN	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Paraesthesia / SOLES TINGLING	03DEC2018 (127)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Rhinorrhoea / RHINNORRHEA	03DEC2018 (127)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER	04DEC2018 (128)	04DEC2018 (128)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	07JAN2019 (162)		Grade 2	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0001	ADIPemPlatinum	Yes	Injury, poisoning and procedural complications / Laceration / R, FOREARM SKIN TEAR	21JAN2019 (176)	21JAN2019 (176)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / SEVERE PAIN RIGHT CHEST WALL	04FEB2019 (190)	07FEB2019 (193)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALAEMIA	07FEB2019 (193)	22FEB2019 (208)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / SEVERE NON-CARDIAC CENTRAL CHEST PAIN	11FEB2019 (197)	25FEB2019 (211)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	25FEB2019 (211)	04MAR2019 (218)	Grade 1	Resolved with Sequelae	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Lower respiratory tract infection / CHEST INFECTION	04MAR2019 (218)	08MAR2019 (222)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0001	ADIPemPlatinum	Yes	Cardiac disorders / Angina pectoris / CARDIAC CHEST PAIN	24MAR2019 (238)	24MAR2019 (238)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0305-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	29JUN2019 (6)	15JUL2019 (22)	Grade 1	Not Resolved	None	Unlikely / Possibly / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHOEA	30JUN2019 (7)		Grade 2	Ongoing	Medication	Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	30JUN2019 (7)		Grade 1	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	12JUL2019 (19)	19JUL2019 (26)	Grade 2	Resolved	Other: CHEMO WITHHELD UNTIL NOT CLINICALLY SIGNIFICANT	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	12JUL2019 (19)		Grade 2	Ongoing	Other: CHEMO WITH HELD UNTIL NOT CLINICALLY SIGNIFICANT	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	13JUL2019 (20)	14JUL2019 (21)	Grade 1	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	Yes
			General disorders and administration site conditions / Fatigue / FATIGUE	16JUL2019 (23)		Grade 2	Ongoing	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	22JUL2019 (29)	12AUG2019 (50)	Grade 2	Resolved	Other: REFERRED TO LOCAL GP AND HOSPITAL FOR TRANSFUSION	Unrelated / Possibly / Probably / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutrophilia / BLOOD AND LYMPHATIC SYSTEM DISORDERS - NEUTROPHILIA	22JUL2019 (29)		Grade 1	Ongoing	None	Unrelated / Probably / Possibly / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	27JUL2019 (34)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0002	PlaceboPemPlatinum	Yes	Injury, poisoning and procedural complications / Fall / FALL	30JUL2019 (37)	30JUL2019 (37)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	12AUG2019 (50)		Grade 1	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	12AUG2019 (50)		Grade 2	Ongoing	Other: GIVEN MEDICAL TREATMENT WHILE AN INPATIENT	Unrelated / Unrelated / Not Applicable / Possibly	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	13AUG2019 (51)	13AUG2019 (51)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization; Other: BLOOD TRANSFUSION	Unrelated / Possibly / Not Applicable / Possibly	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Metabolism and nutrition disorders / Fluid overload / FLUID OVERLOAD	13AUG2019 (51)		Grade 1	Ongoing	None	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	14AUG2019 (52)	15AUG2019 (53)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Probably	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0002	PlaceboPemPlatinum	Yes	Infections and infestations / Urinary tract infection / URINARY TRACT INFECTION	14AUG2019 (52)		Grade 3	Ongoing	Medication	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
0305-0004	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	26MAR2020 (4)		Grade 1	Not Resolved	Medication	Unrelated / Possibly / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / GASTROESOPHAGEAL REFLUX	30MAR2020 (8)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	31MAR2020 (9)		Grade 1	Not Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	01APR2020 (10)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	14APR2020 (23)	22APR2020 (31)	Grade 4	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER	15APR2020 (24)	16APR2020 (25)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0004	ADIPemPlatinum	Yes	Vascular disorders / Orthostatic hypotension / POSTURAL HYPOTENSION	07MAY2020 (46)	20MAY2020 (59)	Grade 2	Resolved	Other: HYPERTENSIVE MEDICATION CEASED. CHANGED FROM CISPLATIN TO CARBOPLATIN	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Drug Withdrawn / Missing	Yes
			Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	11MAY2020 (50)		Grade 1	Not Resolved	Medication	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Tachycardia / TACHYCARDIA	17MAY2020 (56)	20MAY2020 (59)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	25MAY2020 (64)	31MAY2020 (70)	Grade 1	Resolved	None	Unrelated / Probably / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	27MAY2020 (66)	01JUN2020 (71)	Grade 1	Resolved	Medication	Unrelated / Unlikely / Possibly / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0004	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANAEMIA	03JUN2020 (73)		Grade 2	Not Resolved	Other: PACKED RED BLOOD CELLS GIVEN	Unrelated / Probably / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Immune system disorders / Anaphylactic reaction / ANAPHYLAXIS	08JUL2020 (108)	08JUL2020 (108)	Grade 4	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Definitely / Unrelated / Unrelated / Unrelated	Drug Interrupted; Drug Withdrawn / Drug Withdrawn / Not Applicable / Drug Withdrawn	Yes
0305-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	25NOV2020 (10)		Grade 1	Not Resolved	None	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Dehydration / DEHYDRATION	26NOV2020 (11)	26NOV2020 (11)	Grade 2	Resolved	Other: INTRAVENOUS HYDRATION	Unlikely / Unlikely / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Neutrophil count decreased / NEUTROPHIL COUNT DECREASED	10DEC2020 (25)	16DEC2020 (31)	Grade 3	Resolved	None	Unlikely / Probably / Definitely / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Missing	No
			Gastrointestinal disorders / Enterocolitis / ENTEROCOLITIS	20DEC2020 (35)	24DEC2020 (39)	Grade 3	Resolved with Sequelae	Medication; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Possibly / Possibly / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Missing	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0005	ADIPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	20DEC2020 (35)	07JAN2021 (53)	Grade 1	Resolved	Medication	Unlikely / Unlikely / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Paralysis recurrent laryngeal nerve / RECURRENT LARYNGEAL NERVE PALSY	23DEC2020 (38)		Grade 2	Not Resolved	Other: SPEECH THERAPY INVESTIGATIONS/CONSULTATIONS	Unlikely / Unlikely / Unlikely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALEMIA	25DEC2020 (40)	25DEC2020 (40)	Grade 4	Resolved with Sequelae	Medication	Unlikely / Unlikely / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
			Gastrointestinal disorders / Enterocolitis / ENTEROCOLITIS	25DEC2020 (40)	13JAN2021 (59)	Grade 2	Resolved	Medication; Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Possibly / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	Yes
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALEMIA	26DEC2020 (41)	29DEC2020 (44)	Grade 3	Resolved with Sequelae	Medication	Unlikely / Unlikely / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypophosphataemia / HYPOPHOSPHATEMIA	26DEC2020 (41)	29DEC2020 (44)	Grade 3	Resolved	Medication	Unlikely / Unlikely / Probably / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0305-0005	ADIPemPlatinum	Yes	Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESEMIA	28DEC2020 (43)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypokalaemia / HYPOKALEMIA	30DEC2020 (45)	03JAN2021 (49)	Grade 2	Resolved	Medication	Unlikely / Unlikely / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
			Infections and infestations / Mucosal infection / MUCOSAL INFECTION	30DEC2020 (45)		Grade 3	Not Resolved	Medication	Unlikely / Possibly / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No
0502-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	07OCT2019 (6)	12OCT2019 (11)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Weight decreased / WEIGHT LOSS	11OCT2019 (10)	18OCT2019 (17)	Grade 1	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	26OCT2019 (25)	01NOV2019 (31)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Weight decreased / WEIGHT LOSS	31OCT2019 (30)	01NOV2019 (31)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0001	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	17NOV2019 (47)	23NOV2019 (53)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	07DEC2019 (67)	12DEC2019 (72)	Grade 2	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	29DEC2019 (89)	09JAN2020 (100)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	29DEC2019 (89)	10JAN2020 (101)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Syncope / FAINT	23JAN2020 (114)	23JAN2020 (114)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Nervous system disorders / Paraesthesia / HYPOAESTHESIA HANDS AND FEET	07FEB2020 (129)	14FEB2020 (136)	Grade 2	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Musculoskeletal pain / SCAPULAR PAIN	28FEB2020 (150)	06MAR2020 (157)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0001	ADIPemPlatinum	Yes	Nervous system disorders / Syncope / FAINT	27MAR2020 (178)	27MAR2020 (178)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / PERIPHERAL NEUROPATHY	10APR2020 (192)	29APR2020 (211)	Grade 2	Resolved	Other: TREATMENT NOT CARRIED OUT	Unrelated / Unrelated / Possibly / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIE	17APR2020 (199)	30APR2020 (212)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Neuropathy peripheral / NEUROPATHY	30APR2020 (212)		Grade 3	Ongoing	Other: TREATMENT NOT PERFORMED EXPECTS NEUROLOGICAL EXAMINATION	Unrelated / Possibly / Not Applicable	Dose Not Changed; Drug Withdrawn / Not Applicable / Not Applicable / Not Applicable	No
0502-0002	ADIPemPlatinum	Yes	Gastrointestinal disorders / Dyspepsia / BURNING IN THE STOMACH	25OCT2019 (5)	30OCT2019 (10)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0002	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	25OCT2019 (5)	31OCT2019 (11)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIE	11NOV2019 (22)	18NOV2019 (29)	Grade 3	Resolved	Other: DELAY CT	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA G2	09DEC2019 (50)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Dysgeusia / DISGEUSIA	17DEC2019 (58)	07JAN2020 (79)	Grade 1	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Breath sounds abnormal / RESPIRATORY NOISES AT THE LEFT BASE OF THE LUNG	30DEC2019 (71)	07JAN2020 (79)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Gastritis / GASTRITIS	14JAN2020 (86)	22JAN2020 (94)	Grade 2	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Missing	No
			Nervous system disorders / Paraesthesia / RIGHT ARM AND THREE FINGERS PARAESTHESIA	01FEB2020 (104)	01FEB2020 (104)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0002	ADIPemPlatinum	Yes	Nervous system disorders / Dysgeusia / PERSISTENT DISGEUSIA	10FEB2020 (113)	19FEB2020 (122)	Grade 2	Resolved		Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14APR2020 (177)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0502-0003	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	21MAR2020 (4)	02APR2020 (16)	Grade 2	Resolved	Medication	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Missing	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / BILATERAL PULMONARY THROMBOEMBOLISM	23APR2020 (37)	04MAY2020 (48)	Grade 4	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
0502-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	02FEB2021 (7)		Grade 2	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	19FEB2021 (24)	14MAY2021 (108)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Reduced	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	20FEB2021 (25)	04MAR2021 (37)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIE	02MAR2021 (35)	30APR2021 (94)	Grade 2	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	11MAR2021 (44)	21APR2021 (85)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	12MAR2021 (45)	07APR2021 (71)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed; Drug Interrupted / Dose Not Changed; Drug Interrupted	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	08APR2021 (72)	14MAY2021 (108)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	22APR2021 (86)	30APR2021 (94)	Grade 3	Resolved	Medication	Unrelated / Unlikely / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Drug Withdrawn	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0004	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	14MAY2021 (108)	28MAY2021 (122)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Drug Withdrawn	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	14MAY2021 (108)	28MAY2021 (122)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Drug Withdrawn	No
			Gastrointestinal disorders / Gastroesophageal reflux disease / GASTROESOPHAGEAL REFLUX	03JUN2021 (128)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	17JUN2021 (142)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Metabolism and nutrition disorders / Hyperuricaemia / HYPERURICEMIA	08JUL2021 (163)	22JUL2021 (177)	Grade 1	Resolved	Medication	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Arthritis / ARTHRITIS	12JUL2021 (167)	19JUL2021 (174)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Gastrointestinal pain / GASTROINTESTINAL PAIN	15JUL2021 (170)		Grade 2	Ongoing	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0004	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Lymphadenopathy / LYMPHADENOPATHY OF THE RIGHT MAMMARY CHAIN	02SEP2021 (219)		Grade 3	Ongoing	Other: RADIOTHER APY	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable	No
			Injury, poisoning and procedural complications / Vaccination complication / FEVER DUE TO VACCINATION FOR COVID	30SEP2021 (247)	30SEP2021 (247)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	06OCT2021 (253)	12OCT2021 (259)	Grade 1	Resolved		Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Missing / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / ANTHRAGIA	15OCT2021 (262)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	18NOV2021 (296)		Grade 1	Ongoing	Medication	Unrelated / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable	No
0502-0005	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	27MAR2021 (4)	05AUG2021 (135)	Grade 1	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0005	ADIPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	01APR2021 (9)	08APR2021 (16)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Dry mouth / DRY MOUTH	04JUN2021 (73)	17JUN2021 (86)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	10JUN2021 (79)	17JUN2021 (86)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / ABDOMINAL PAIN	01SEP2021 (162)	09SEP2021 (170)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	01SEP2021 (162)	09SEP2021 (170)	Grade 1	Resolved	None	Unlikely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Dyspepsia / DYSPEPSIA	09SEP2021 (170)	16SEP2021 (177)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0006	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	01APR2021 (2)	19AUG2021 (142)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Reduced / Dose Not Changed / Dose Reduced	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	01APR2021 (2)	19AUG2021 (142)	Grade 2	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Reduced / Dose Not Changed / Dose Reduced	No
			Respiratory, thoracic and mediastinal disorders / Epistaxis / EPISTAXIS	28APR2021 (29)	28APR2021 (29)	Grade 1	Resolved	None	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	20MAY2021 (51)	27MAY2021 (58)	Grade 3	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	20MAY2021 (51)		Grade 2	Ongoing	Medication	Unrelated / Possibly / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	29JUN2021 (91)	08JUL2021 (100)	Grade 1	Resolved	None	Unrelated / Unlikely / Not Applicable / Unlikely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	09JUL2021 (101)	22JUL2021 (114)	Grade 1	Resolved	None	Unlikely / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0006	PlaceboPemPlatinum	Yes	Infections and infestations / Conjunctivitis / CONJUNCTIVITIS	09JUL2021 (101)	22JUL2021 (114)	Grade 1	Resolved	None	Unrelated / Probably / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0502-0008	ADIPemPlatinum	Yes	General disorders and administration site conditions / Chest pain / THORACIC PAIN	09JUN2021 (-7)		Grade 2	Not Resolved	Medication	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	23JUN2021 (8)	26JUN2021 (11)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	23JUN2021 (8)	26JUN2021 (11)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain upper / STOMACH PAIN	24JUN2021 (9)	01JUL2021 (16)	Grade 2	Resolved	Medication	Unrelated / Probably / Not Applicable / Probably	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	24JUN2021 (9)	01JUL2021 (16)	Grade 2	Resolved	Medication	Probably / Probably / Probably / Probably	Drug Interrupted / Drug Interrupted / Drug Interrupted / Drug Interrupted	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	25JUN2021 (10)	01JUL2021 (16)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Probably	Dose Not Changed / Dose Reduced / Dose Reduced / Dose Reduced	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0008	ADIPemPlatinum	Yes	General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	25JUN2021 (10)		Grade 1	Ongoing	Medication	Unrelated / Probably / Not Applicable / Probably	Unknown / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Pyrexia / FEVER UP TO 37.5 °C	10JUL2021 (25)	21JUL2021 (36)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Injury, poisoning and procedural complications / Femur fracture / PERTROCANTRERIC FRACTURE	10JUL2021 (25)		Grade 1	Ongoing	None	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	15JUL2021 (30)	22JUL2021 (37)	Grade 2	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Drug Interrupted / Dose Not Changed; Drug Interrupted / Dose Not Changed / Drug Interrupted	No
			Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	11NOV2021 (149)		Grade 2	Ongoing	None	Probably / Not Applicable / Not Applicable / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0502-0010	ADIPemPlatinum	Yes	Vascular disorders / Hypertension / HYPERTENSION	30AUG2021 (15)	30AUG2021 (15)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	23OCT2021 (69)	30OCT2021 (76)	Grade 2	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Dose Reduced / Dose Reduced / Not Applicable	No
0502-0011	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	28OCT2021 (74)	11NOV2021 (88)	Grade 1	Resolved	Medication	Not Applicable / Unrelated / Not Applicable / Probably	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Reduced	No
0503-0001	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Musculoskeletal chest pain / CHEST WALL PAIN	05JUN2019 (10)		Grade 3	Ongoing	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Blood creatinine increased / INCREASE CREATININE	08JUL2019 (43)	28AUG2019 (94)	Grade 1	Resolved	None	Unrelated / Unrelated / Probably / Not Applicable	Dose Not Changed / Dose Not Changed; Drug Interrupted / Drug Interrupted / Not Applicable	No
			Vascular disorders / Deep vein thrombosis / PARTIAL SUPERIOR CAVA THROMBOSIS AND DISTAL TRACT OF THE ANONYMOUS VENOUS TRUNK	16JUL2019 (51)	30JAN2020 (249)	Grade 2	Resolved	Medication	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0503-0003	PlaceboPemPlatinum	Yes	Nervous system disorders / Syncope / SYNCOPAL EPISODE	06OCT2019 (12)	07OCT2019 (13)	Grade 4	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Missing	Yes
			Infections and infestations / Septic shock / SEPTIC SHOCK	14OCT2019 (20)	14OCT2019 (20)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Withdrawn / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
0505-0001	PlaceboPemPlatinum	Yes	Investigations / Blood uric acid increased / URIC ACID INCREASE	27APR2020 (1)	19MAY2020 (23)	Grade 1	Resolved	Medication	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	27APR2020 (1)		Grade 1	Not Resolved	None	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	03MAY2020 (7)	08MAY2020 (12)	Grade 2	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA (HB 8.8G/DL REF 13.0-18.0)	18MAY2020 (22)		Grade 2	Resolving	Medication	Unlikely / Definitely / Not Applicable / Definitely	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No

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Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0505-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	05JUN2020 (40)	12JUN2020 (47)	Grade 1	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / ANOREXIA	05JUN2020 (40)	12JUN2020 (47)	Grade 1	Resolved	Medication	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Not Applicable	No
0505-0002	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	01FEB2021 (22)	09FEB2021 (30)	Grade 1	Resolved	Medication	Probably / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASE	01FEB2021 (22)	22FEB2021 (43)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Aspartate aminotransferase increased / ASPARTATE AMINOTRANSFERASE INCREASE	01FEB2021 (22)	22FEB2021 (43)	Grade 1	Resolved	None	Probably / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0505-0002	PlaceboPemPlatinum	Yes	Investigations / Gamma-glutamyltransferase increased / GAMMA GLUTAMYL TRANSFERASE INCREASE	01FEB2021 (22)	15MAR2021 (64)	Grade 1	Resolved	None	Probably / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	25FEB2021 (46)	25FEB2021 (46)	Grade 1	Resolved	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Platelet count decreased / PLATELET NUMBER DECREASE	09MAR2021 (58)	15MAR2021 (64)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09MAR2021 (58)	11MAY2021 (121)	Grade 1	Resolved with Sequelae	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Platelet count decreased / PLATELET NUMBER DECREASE	20APR2021 (100)	26APR2021 (106)	Grade 1	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	11MAY2021 (121)	17MAY2021 (127)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Investigations / Platelet count decreased / PLATELET NUMBER DECREASE	11MAY2021 (121)	17MAY2021 (127)	Grade 2	Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0505-0002	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	11MAY2021 (121)	07JUL2021 (178)	Grade 2	Resolved with Sequelae	Medication	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hypocalcaemia / HYPOCALCEMIA	17MAY2021 (127)	24MAY2021 (134)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hypomagnesaemia / HYPOMAGNESIEMIA	17MAY2021 (127)	24MAY2021 (134)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Metabolism and nutrition disorders / Hyposideraemia / HYPOSIDEREMIA	19MAY2021 (129)		Grade 3	Resolving	Medication	Unlikely / Probably / Probably / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			General disorders and administration site conditions / Pain / WORSENING OF DISEASE RELATED PAIN	07JUN2021 (148)		Grade 2	Resolving	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYPNEA	01JUL2021 (172)		Grade 2	Resolving	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0505-0002	PlaceboPemPlatinum	Yes	Investigations / Blood alkaline phosphatase increased / ALKALINE PHOSPHATASE INCREASE	05JUL2021 (176)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Investigations / Gamma-glutamyltransferase increased / GAMMA GLUTAMYL TRANSFERASE INCREASE	05JUL2021 (176)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Investigations / Platelet count increased / PLATELET NUMBER INCREASE	05JUL2021 (176)		Grade 1	Resolving	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	07JUL2021 (178)	12JUL2021 (183)	Grade 3	Resolved	Medication; Surgical/ Diagnostic Procedure; Other: BLOOD TRANSFUSION	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Missing	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	12JUL2021 (183)		Grade 2	Ongoing	Medication	Unrelated / Definitely / Definitely / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Missing	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0001	ADIPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / ALANINE AMINOTRANSFERASE INCREASED	14JUN2019 (8)	20JUN2019 (14)	Grade 3	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	14JUN2019 (8)	20JUN2019 (14)	Grade 2	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Haematuria / HEMATURIA	06JUL2019 (30)	07JUL2019 (31)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	26JUL2019 (50)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Psychiatric disorders / Panic attack / PANIC ATTACK	04AUG2019 (59)	04AUG2019 (59)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Ear and labyrinth disorders / Deafness / HEARING LOSS	04AUG2019 (59)		Grade 1	Not Resolved	None	Unrelated / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0001	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Pleural effusion / PLEURAL EFFUSION	21AUG2019 (76)	31AUG2019 (86)	Grade 3	Resolved	Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
0506-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	20JUN2019 (4)	04JUL2019 (18)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	20JUN2019 (4)	03AUG2019 (48)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	25JUN2019 (9)	26JUN2019 (10)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Stomatitis / MOUTH SORES	25JUN2019 (9)	04JUL2019 (18)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	30JUN2019 (14)	01AUG2019 (46)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0002	PlaceboPemPlatinum	Yes	Ear and labyrinth disorders / Tinnitus / TINNITUS	05JUL2019 (19)		Grade 1	Ongoing	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Metabolism and nutrition disorders / Hypocalcaemia / HYPOCALCEMIA	25JUL2019 (39)	07AUG2019 (52)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Renal and urinary disorders / Pollakiuria / POLLAKIURIA	09AUG2019 (54)	15AUG2019 (60)	Grade 1	Resolved	None	Probably / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	09AUG2019 (54)	17AUG2019 (62)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	09AUG2019 (54)	25AUG2019 (70)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	17AUG2019 (62)	31AUG2019 (76)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	01SEP2019 (77)	08SEP2019 (84)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	01SEP2019 (77)	13SEP2019 (89)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Psychiatric disorders / Depression / DEPRESSION	01SEP2019 (77)	23OCT2019 (129)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	02SEP2019 (78)	10SEP2019 (86)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Fatigue / FATIGUE	09SEP2019 (85)	23OCT2019 (129)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	14SEP2019 (90)	28SEP2019 (104)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Nausea / NAUSEA	29SEP2019 (105)	07OCT2019 (113)	Grade 1	Resolved	None	Probably / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	27NOV2019 (164)	31DEC2019 (198)	Grade 1	Resolved	None	Definitely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0002	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Arthralgia / ARTHRALGIA	27NOV2019 (164)		Grade 1	Not Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0506-0004	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	29MAR2020 (5)		Grade 1	Not Resolved	None	Not Applicable / Probably / Probably / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	11APR2020 (18)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable	Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMIT	20APR2020 (27)	23APR2020 (30)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Respiratory failure / RESPIRATORY FAILURE (DISEASE RELATED)"	05MAY2020 (42)		Grade 4	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0506-0005	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	15MAY2020 (10)	15MAY2020 (10)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0005	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	22MAY2020 (17)	25MAY2020 (20)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	26MAY2020 (21)	27MAY2020 (22)	Grade 1	Resolved	None	Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed /	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	01JUN2020 (27)	08JUN2020 (34)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed /	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPHENIA	03JUN2020 (29)	09JUN2020 (35)	Grade 4	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Not Applicable / Dose Not Changed / Not Applicable / Dose Not Changed /	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	03JUN2020 (29)	09JUN2020 (35)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEHMIA	09JUN2020 (35)	03JUL2020 (59)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	09JUN2020 (35)	19JUL2020 (75)	Grade 2	Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0005	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Diarrhoea / DIARRHEA	01JUL2020 (57)	02JUL2020 (58)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Headache / HEADACHE	09JUL2020 (65)	10JUL2020 (66)	Grade 2	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	09JUL2020 (65)	01AUG2020 (88)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	03AUG2020 (90)	06AUG2020 (93)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	05AUG2020 (92)	06AUG2020 (93)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	26AUG2020 (113)	06OCT2020 (154)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	15OCT2020 (163)	16OCT2020 (164)	Grade 1	Resolved	None	Definitely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0005	PlaceboPemPlatinum	Yes	Nervous system disorders / Sciatica / SCIATICA	12NOV2020 (191)	18NOV2020 (197)	Grade 1	Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	25DEC2020 (234)	09JAN2021 (249)	Grade 1	Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / ARTHRALGIA	25DEC2020 (234)		Grade 1	Not Resolved	Medication	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	20JAN2021 (260)	21JAN2021 (261)	Grade 1	Resolved	None	Possibly / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0506-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	29AUG2020 (4)	30AUG2020 (5)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Metabolism and nutrition disorders / Decreased appetite / NO APPETITE	29AUG2020 (4)	30AUG2020 (5)	Grade 1	Resolved	None	Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Pyrexia / FEVER	05SEP2020 (11)	06SEP2020 (12)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	19SEP2020 (25)	21SEP2020 (27)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APETITE	10OCT2020 (46)	16OCT2020 (52)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Fatigue / FATIGUE	10OCT2020 (46)	03NOV2020 (70)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Pyrexia / FEVER	21OCT2020 (57)	02NOV2020 (69)	Grade 1	Resolved	None	Possibly /	Dose Not Changed /	No
			Metabolism and nutrition disorders / Decreased appetite / LOSS OF APETITE	22OCT2020 (58)	03NOV2020 (70)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Pulmonary embolism / PULMONARY THROMBOEMBOLISM	11NOV2020 (78)		Grade 1	Not Resolved	Medication	Unrelated /	Not Applicable /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0006	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC THORACIC PAIN	14DEC2020 (111)		Grade 1	Not Resolved	None	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	22DEC2020 (119)		Grade 2	Not Resolved	None	Definitely / Definitely / Definitely / Definitely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	06FEB2021 (165)	12FEB2021 (171)	Grade 1	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
0506-0008	PlaceboPemPlatinum	Yes	Nervous system disorders / Dizziness / DIZZINESS	14APR2021 (8)	14APR2021 (8)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC LEFT THORACIC PAIN	21APR2021 (15)	27APR2021 (21)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	21APR2021 (15)	06MAY2021 (30)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0008	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	27APR2021 (21)	28APR2021 (22)	Grade 3	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Eye disorders / Lacrimation increased / TEARING	27APR2021 (21)	05MAY2021 (29)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	28APR2021 (22)	04MAY2021 (28)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Arthralgia / OSTEOARTICULAR PAINS	07MAY2021 (31)	11MAY2021 (35)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	07MAY2021 (31)	14MAY2021 (38)	Grade 2	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	07MAY2021 (31)	14MAY2021 (38)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal pain / ADDOMINAL PAIN	09MAY2021 (33)	16MAY2021 (40)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0008	PlaceboPemPlatinum	Yes	Musculoskeletal and connective tissue disorders / Arthralgia / OSTEOARTICULAR PAINS	12MAY2021 (36)	26MAY2021 (50)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Unknown / Unknown / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	15MAY2021 (39)	17MAY2021 (41)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	15MAY2021 (39)	05JUN2021 (60)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Abdominal pain / ADDOMINAL PAIN	19MAY2021 (43)	26MAY2021 (50)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	06JUN2021 (61)	10JUN2021 (65)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMIT	09JUN2021 (64)	09JUN2021 (64)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	11JUN2021 (66)	03SEP2021 (150)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0008	PlaceboPemPlatinum	Yes	Eye disorders / Lacrimation increased / TEARING	12JUN2021 (67)	20JUL2021 (105)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Headache / HEADACHE	15JUN2021 (70)	18JUN2021 (73)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Nervous system disorders / Headache / HEADACHE	23JUN2021 (78)	20JUL2021 (105)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	01JUL2021 (86)	22JUL2021 (107)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	01JUL2021 (86)		Grade 2	Not Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Eye disorders / Lacrimation increased / TEARING	06AUG2021 (122)		Grade 1	Not Resolved	Medication	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	27AUG2021 (143)		Grade 1	Not Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0009	ADIPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	12JUN2021 (4)		Grade 1	Not Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	12JUN2021 (4)		Grade 1	Not Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DISPNEA	12JUN2021 (4)		Grade 1	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	14JUN2021 (6)	14JUN2021 (6)	Grade 1	Resolved	Medication	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Mucosal inflammation / MUCOSITIS	23JUN2021 (15)	14JUL2021 (36)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29JUN2021 (21)	10AUG2021 (63)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Reduced	No
			Infections and infestations / Pneumonia / PNEUMONIA	21JUL2021 (43)	03AUG2021 (56)	Grade 3	Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0009	ADIPemPlatinum	Yes	General disorders and administration site conditions / Fatigue / FATIGUE	21JUL2021 (43)		Grade 2	Not Resolved	None	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	24AUG2021 (77)	31AUG2021 (84)	Grade 2	Resolved	None	Unrelated /	Not Applicable /	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	24AUG2021 (77)	31AUG2021 (84)	Grade 2	Resolved	Medication	Definitely /	Drug Interrupted /	No
			Infections and infestations / Infection / INFECTION (UNKNOWN ORIGIN)	22SEP2021 (106)		Grade 2	Not Resolved	None	Definitely /	Drug Interrupted /	No
			Metabolism and nutrition disorders / Hyponatraemia / HYPONATREMIA	23SEP2021 (107)	28SEP2021 (112)	Grade 3	Resolved	None	Unrelated /	Dose Not Changed /	No
0506-0010	ADIPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON-CARDIAC THORACIC PAIN.	03AUG2021 (7)	03AUG2021 (7)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0010	ADIPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DISPNEA	03AUG2021 (7)	03AUG2021 (7)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Cardiac disorders / Pericarditis / PERICARDITIS	03AUG2021 (7)	04AUG2021 (8)	Grade 2	Resolved	Medication; Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Dose Not Changed; Drug Interrupted / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	25AUG2021 (29)	31AUG2021 (35)	Grade 2	Resolved	Medication	Definitely / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	25AUG2021 (29)		Grade 3	Not Resolved	Medication	Definitely / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	02SEP2021 (37)	05SEP2021 (40)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			General disorders and administration site conditions / Fatigue / FATIGUE	05SEP2021 (40)	22NOV2021 (118)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Gastrointestinal disorders / Vomiting / VOMIT	14SEP2021 (49)	15SEP2021 (50)	Grade 1	Resolved	None	Definitely / Possibly / Possibly / Not Applicable / Possibly	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0506-0010	ADIPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	14SEP2021 (49)	24SEP2021 (59)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	28OCT2021 (93)	02NOV2021 (98)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	08NOV2021 (104)	13NOV2021 (109)	Grade 1	Resolved	Medication	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	25NOV2021 (121)	26NOV2021 (122)	Grade 1	Resolved	Medication	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	25NOV2021 (121)	30NOV2021 (126)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
0508-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Constipation / CONSTIPATION	20MAY2020 (3)		Grade 1	Not Resolved	None	Probably /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	01JUN2020 (15)		Grade 1	Not Resolved	None	Definitely /	Dose Not Changed /	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0508-0001	PlaceboPemPlatinum	Yes	Nervous system disorders / Headache / HEADACHE	30JUN2020 (44)	01JUL2020 (45)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Not Applicable / Dose Not Changed / Dose Not Changed	No
			Musculoskeletal and connective tissue disorders / Bone pain / BONE PAIN	30JUN2020 (44)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	30JUN2020 (44)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Drug Interrupted / Drug Interrupted / Not Applicable / Drug Interrupted	No
			Gastrointestinal disorders / Nausea / NAUSEA	01JUL2020 (45)	31JUL2020 (75)	Grade 1	Resolved with Sequelae	None	Probably / Definitely / Definitely / Definitely	Drug Interrupted / Drug Interrupted / Drug Interrupted / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	31JUL2020 (75)		Grade 2	Not Resolved	None	Unrelated / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
			Respiratory, thoracic and mediastinal disorders / Pneumothorax / PNEUMOTHORAX	05AUG2020 (80)		Grade 3	Not Resolved	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Not Applicable / Unrelated	Not Applicable / Drug Interrupted; Drug Withdrawn / Not Applicable / Not Applicable	Yes

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0509-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	18SEP2018 (1)	26SEP2018 (9)	Grade 1	Resolved	None	Definitely / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Missing / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	10OCT2018 (23)	05DEC2018 (79)	Grade 1	Resolved	None	Unrelated / Probably / Probably / Not Applicable	Not Applicable / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Back pain / LUMBAR PAIN	25OCT2018 (38)	26OCT2018 (39)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	07NOV2018 (51)	14NOV2018 (58)	Grade 2	Resolved	None	Unlikely / Probably / Probably / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Creatinine renal clearance increased / CREATININE CLEARANCE INCREASE	21NOV2018 (65)		Grade 2	Not Resolved	None	Unrelated / Unrelated / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
0510-0001	PlaceboPemPlatinum	Yes	Investigations / Blood pressure increased / BLOOD PRESSURE RISE	28FEB2020 (3)	28FEB2020 (3)	Grade 2	Resolved	Medication	Unrelated / Not Applicable / Not Applicable / Not Applicable	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0510-0001	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	23MAR2020 (27)	27MAR2020 (31)	Grade 1	Resolved	Medication	Unrelated / Possibly / Not Applicable / Possibly	Dose Not Changed / Not Applicable / Not Applicable / Not Applicable	No
			Gastrointestinal disorders / Vomiting / VOMITING	07APR2020 (42)	10APR2020 (45)	Grade 1	Resolved	None	Possibly / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Infections and infestations / Dysentery / ACUTE DYSENTERY	07APR2020 (42)	10APR2020 (45)	Grade 1	Resolved	None	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Not Applicable / Dose Not Changed	No
0511-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	23APR2019 (15)	29APR2019 (21)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	23APR2019 (15)	29APR2019 (21)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	23APR2019 (15)	29APR2019 (21)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	29APR2019 (21)	02MAY2019 (24)	Grade 4	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Dose Not Changed	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	02MAY2019 (24)	06MAY2019 (28)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	02MAY2019 (24)	06MAY2019 (28)	Grade 3	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	14MAY2019 (36)	21MAY2019 (43)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	11JUN2019 (64)	17JUN2019 (70)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Missing	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	25JUN2019 (78)	03SEP2019 (148)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	02JUL2019 (85)	08JUL2019 (91)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	02JUL2019 (85)	23JUL2019 (106)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	23JUL2019 (106)	29JUL2019 (112)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	23JUL2019 (106)	29JUL2019 (112)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	23JUL2019 (106)	30JUL2019 (113)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	29JUL2019 (112)	30JUL2019 (113)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	29JUL2019 (112)		Grade 1	Not Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	31JUL2019 (114)	02AUG2019 (116)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	13AUG2019 (127)	20AUG2019 (134)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	13AUG2019 (127)	03SEP2019 (148)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	20AUG2019 (134)	03SEP2019 (148)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	27AUG2019 (141)	03SEP2019 (148)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Blood creatinine decreased / CREATININA DECREASED	03SEP2019 (148)	10SEP2019 (155)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Neoplasms benign, malignant and unspecified (incl cysts and polyps) / Tumour pain / TUMOR PAIN (CHEST)	03SEP2019 (148)	05MAR2020 (332)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	17SEP2019 (162)	26SEP2019 (171)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	03OCT2019 (178)	21NOV2019 (227)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0001	ADIPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	17OCT2019 (192)	24OCT2019 (199)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Cardiac disorders / Extrasystoles / EXTRASYSTOLES	17OCT2019 (192)	31OCT2019 (206)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Nervous system disorders / Dizziness / DIZZINESS	24OCT2019 (199)	31OCT2019 (206)	Grade 2	Resolved	Other: NO THERAPY	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Dose Not Changed	No
			Psychiatric disorders / Insomnia / INSOMNIA	21NOV2019 (227)	21JAN2020 (288)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0511-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	21MAY2019 (8)	28MAY2019 (15)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	28MAY2019 (15)	03JUN2019 (21)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	03JUN2019 (21)	04JUN2019 (22)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0002	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Asthenia / ASTHENIA	11JUN2019 (29)	24JUN2019 (42)	Grade 1	Resolved	Medication	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	24JUN2019 (42)	25JUN2019 (43)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	24JUN2019 (42)	25JUN2019 (43)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	29JUN2019 (47)	06AUG2019 (85)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	02JUL2019 (50)	09JUL2019 (57)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	02JUL2019 (50)	27AUG2019 (106)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	09JUL2019 (57)	06AUG2019 (85)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0002	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Decreased appetite / LOSS OF HUNGER	21JUL2019 (69)	30JUL2019 (78)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Leukopenia / LEUKOPENIA	13AUG2019 (92)	27AUG2019 (106)	Grade 2	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	13AUG2019 (92)	27AUG2019 (106)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Dose Not Changed	No
0511-0003	PlaceboPemPlatinum	Yes	Psychiatric disorders / Anxiety / ANXIETY	01AUG2019 (-5)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	20AUG2019 (15)		Grade 1	Not Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASE	24SEP2019 (50)	01OCT2019 (57)	Grade 1	Resolved	None	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	02OCT2019 (58)	22OCT2019 (78)	Grade 1	Resolved	Medication	Definitely / Definitely / Definitely / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0004	PlaceboPemPlatinum	Yes	Investigations / Alanine aminotransferase increased / ALT INCREASED	29SEP2020 (8)	06OCT2020 (15)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Blood bilirubin unconjugated increased / INDIRECT BILIRUBIN INCREASED	29SEP2020 (8)	06OCT2020 (15)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	29SEP2020 (8)	13OCT2020 (22)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Stomatitis / STOMATITIS	06OCT2020 (15)	13OCT2020 (22)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	06OCT2020 (15)	13OCT2020 (22)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Platelet count increased / PLT INCREASED	06OCT2020 (15)	13OCT2020 (22)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	06OCT2020 (15)	20OCT2020 (29)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0004	PlaceboPemPlatinum	Yes	Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	06OCT2020 (15)	20OCT2020 (29)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	13OCT2020 (22)	17DEC2020 (87)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	20OCT2020 (29)	27OCT2020 (36)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	20OCT2020 (29)	27OCT2020 (36)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	20OCT2020 (29)	19JAN2021 (120)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Platelet count decreased / PLATELETS DECREASED	27OCT2020 (36)	17NOV2020 (57)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	17NOV2020 (57)	23NOV2020 (63)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0004	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	17NOV2020 (57)	23NOV2020 (63)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	17NOV2020 (57)	23NOV2020 (63)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	01DEC2020 (71)	17DEC2020 (87)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Blood urea increased / UREA INCREASED	01DEC2020 (71)	17DEC2020 (87)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	29DEC2020 (99)	05JAN2021 (106)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	29DEC2020 (99)		Grade 1	Ongoing	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	12JAN2021 (113)	19JAN2021 (120)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0004	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	12JAN2021 (113)	19JAN2021 (120)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	19JAN2021 (120)	26JAN2021 (127)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	19JAN2021 (120)	02FEB2021 (134)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	19JAN2021 (120)		Grade 2	Ongoing	None	Definitely /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	27JAN2021 (128)	31JAN2021 (132)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09FEB2021 (141)	16FEB2021 (148)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	09FEB2021 (141)	16FEB2021 (148)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0004	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	16FEB2021 (148)		Grade 1	Ongoing	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
0511-0005	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	03NOV2020 (15)	10NOV2020 (22)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	03NOV2020 (15)	17NOV2020 (29)	Grade 1	Resolved	Other: THERAPY POSTPONED BY A WEEK	Definitely / Definitely / Not Applicable / Definitely	Drug Interrupted / Drug Interrupted / Dose Not Changed / Drug Interrupted	No
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	21NOV2020 (33)	25NOV2020 (37)	Grade 2	Resolved	Medication	Definitely / Definitely / Not Applicable / Definitely	Drug Withdrawn / Drug Interrupted / Dose Not Changed / Drug Interrupted	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	10DEC2020 (52)	17DEC2020 (59)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	29DEC2020 (71)	05JAN2021 (78)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	19JAN2021 (92)		Grade 1	Ongoing	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0006	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	22DEC2020 (1)	24DEC2020 (3)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Not Applicable / Unrelated	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	24DEC2020 (3)	29DEC2020 (8)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Gastrointestinal disorders / Nausea / NAUSEA	24DEC2020 (3)	29DEC2020 (8)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	29DEC2020 (8)	05JAN2021 (15)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	05JAN2021 (15)	12JAN2021 (22)	Grade 4	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	05JAN2021 (15)	12JAN2021 (22)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Drug Interrupted / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	05JAN2021 (15)	12JAN2021 (22)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0006	PlaceboPemPlatinum	Yes	Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	12JAN2021 (22)	26JAN2021 (36)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	12JAN2021 (22)	02FEB2021 (43)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	19JAN2021 (29)	26JAN2021 (36)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	19JAN2021 (29)	26JAN2021 (36)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	19JAN2021 (29)	09FEB2021 (50)	Grade 1	Resolved	Medication	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	19JAN2021 (29)	16FEB2021 (57)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	26JAN2021 (36)	02FEB2021 (43)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
05111-0006	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	26JAN2021 (36)	09FEB2021 (50)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Investigations / Gamma-glutamyltransferase increased / GGT INCREASED	26JAN2021 (36)	25MAR2021 (94)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			General disorders and administration site conditions / Asthenia / ASTHENIA	26JAN2021 (36)		Grade 1	Ongoing	None	Definitely /	Dose Not Changed /	No
			Investigations / Blood creatinine increased / CREATININEMIA	02FEB2021 (43)	16FEB2021 (57)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09FEB2021 (50)	16FEB2021 (57)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	09FEB2021 (50)	16FEB2021 (57)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	16FEB2021 (57)	02MAR2021 (71)	Grade 2	Resolved	None	Definitely /	Dose Not Changed /	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0006	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	16FEB2021 (57)	02MAR2021 (71)	Grade 3	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	16FEB2021 (57)	02MAR2021 (71)	Grade 3	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	16FEB2021 (57)	02MAR2021 (71)	Grade 3	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	02MAR2021 (71)	09MAR2021 (78)	Grade 1	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			General disorders and administration site conditions / Non-cardiac chest pain / NON CARDIAC CHEST PAIN	02MAR2021 (71)		Grade 2	Ongoing	Medication	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Leukopenia / LEUCOPENIA	09MAR2021 (78)	25MAR2021 (94)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No
			Blood and lymphatic system disorders / Neutropenia / NEUTROPENIA	09MAR2021 (78)	25MAR2021 (94)	Grade 2	Resolved	None	Definitely / Definitely / Not Applicable / Definitely	Dose Not Changed / Dose Not Changed / Dose Not Changed / Dose Not Changed	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
0511-0006	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	09MAR2021 (78)	25MAR2021 (94)	Grade 2	Resolved with Sequelae	None	Definitely /	Dose Not Changed /	No
			Investigations / Blood bilirubin increased / BILIRUBINA INCREASED	09MAR2021 (78)	25MAR2021 (94)	Grade 1	Resolved	None	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	09MAR2021 (78)	08APR2021 (108)	Grade 2	Resolved	Surgical/ Diagnostic Procedure	Definitely /	Dose Not Changed /	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	08APR2021 (108)		Grade 1	Ongoing	None	Unrelated /	Dose Not Changed /	No
									Unrelated /	Dose Not Changed /	
									Not Applicable /	Dose Not Changed /	
									Unrelated	Dose Not Changed	
1201-0001	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	07NOV2018 (8)	14NOV2018 (15)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH INTERMITTENTLY	07NOV2018 (8)	12DEC2018 (43)	Grade 2	Resolved	None	Unrelated /	Dose Not Changed /	No
			Gastrointestinal disorders / Nausea / NAUSEA	14NOV2018 (15)	20NOV2018 (21)	Grade 1	Resolved	None	Unrelated /	Dose Not Changed /	No
									Not Applicable	Not Applicable	
									Possibly /	Dose Not Changed /	
									Possibly /	Dose Not Changed /	
									Possibly /	Dose Not Changed /	
									Not Applicable	Not Applicable	

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1201-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMITING	14NOV2018 (15)	20NOV2018 (21)	Grade 1	Resolved	None	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Oral candidiasis / ORAL CANDIDIASIS	14NOV2018 (15)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / SKIN RASHES	17NOV2018 (18)	12DEC2018 (43)	Grade 2	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Lip swelling / LIP SWELLING	18NOV2018 (19)	12DEC2018 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea exertional / DYSPNEA ON EXERTION	18NOV2018 (19)	22DEC2018 (53)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	18NOV2018 (19)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Oropharyngeal pain / SORE THROAT	19NOV2018 (20)	12DEC2018 (43)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1201-0001	PlaceboPemPlatinum	Yes	Investigations / Aspartate aminotransferase increased / AST INCREASED	12DEC2018 (43)	14DEC2018 (45)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Alanine aminotransferase increased / ALT INCREASED	12DEC2018 (43)	16JAN2019 (78)	Grade 3	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Possibly / Possibly / Possibly / Not Applicable	Drug Interrupted / Drug Interrupted / Drug Interrupted / Not Applicable	Yes
			Investigations / Aspartate aminotransferase increased / AST INCREASED	14DEC2018 (45)	17DEC2018 (48)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Fatigue / FATIGUE	14DEC2018 (45)	24DEC2018 (55)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	17DEC2018 (48)	20DEC2018 (51)	Grade 2	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Abdominal distension / ABDOMINAL FULLNESS	17DEC2018 (48)	22DEC2018 (53)	Grade 1	Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	20DEC2018 (51)	24DEC2018 (55)	Grade 3	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1201-0001	PlaceboPemPlatinum	Yes	Investigations / Aspartate aminotransferase increased / AST INCREASED	24DEC2018 (55)	02JAN2019 (64)	Grade 2	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Aspartate aminotransferase increased / AST INCREASED	02JAN2019 (64)	16JAN2019 (78)	Grade 1	Resolved	Medication	Possibly / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Mycoplasma infection / MYCOPLASMA INFECTION	09JAN2019 (71)	16JAN2019 (78)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	16JAN2019 (78)	23JAN2019 (85)	Grade 3	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASED	16JAN2019 (78)	31JAN2019 (93)	Grade 2	Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Blood creatinine increased / CREATININE INCREASED	16JAN2019 (78)		Grade 1	Not Resolved	None	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Reduced / Not Applicable	No
			General disorders and administration site conditions / Oedema / PITTING EDEMA	20JAN2019 (82)		Grade 2	Not Resolved	Medication	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1201-0001	PlaceboPemPlatinum	Yes	Blood and lymphatic system disorders / Anaemia / ANEMIA	23JAN2019 (85)	31JAN2019 (93)	Grade 2	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Pneumonia / PNEUMONIA	31JAN2019 (93)	04FEB2019 (97)	Grade 5	Fatal	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Drug Interrupted / Not Applicable / Not Applicable / Not Applicable	Yes
1206-0001	PlaceboPemPlatinum	Yes	Respiratory, thoracic and mediastinal disorders / Wheezing / EXPIRATORY WHEEZING	08FEB2018 (3)	30MAR2018 (53)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	10FEB2018 (5)	06MAR2018 (29)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Angular cheilitis / ANGULAR CHEILITIS	13MAR2018 (36)	27MAR2018 (50)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS	13MAR2018 (36)	27MAR2018 (50)	Grade 1	Resolved	Medication	Unrelated / Possibly / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Polyuria / POLYURIA	03APR2018 (57)	15MAY2018 (99)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0001	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Nausea / NAUSEA	12APR2018 (66)	13APR2018 (67)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Constipation / CONSTIPATION	02MAY2018 (86)		Grade 1	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			General disorders and administration site conditions / Malaise / MALAISE	15MAY2018 (99)	19MAY2018 (103)	Grade 1	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITUS	21MAY2018 (105)	21MAY2018 (105)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Gastrointestinal disorders / Nausea / NAUSEA	22MAY2018 (106)	23MAY2018 (107)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Musculoskeletal and connective tissue disorders / Pain in extremity / RIGHT ARM PAIN	09JUL2018 (154)	12JUL2018 (157)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Nervous system disorders / Headache / HEADACHE	09JUL2018 (154)	12JUL2018 (157)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0001	PlaceboPemPlatinum	Yes	General disorders and administration site conditions / Pyrexia / FEVER	09JUL2018 (154)	24JUL2018 (169)	Grade 1	Resolved	Medication; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Gastrointestinal disorders / Nausea / NAUSEA	12JUL2018 (157)	14JUL2018 (159)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Dyspnoea / DYSPNEA	12JUL2018 (157)	15JUL2018 (160)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Metabolism and nutrition disorders / Decreased appetite / POOR APPETITE	12JUL2018 (157)	24JUL2018 (169)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Cough / COUGH	12JUL2018 (157)	24JUL2018 (169)	Grade 3	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / PRURITIS	16JUL2018 (161)	24JUL2018 (169)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Respiratory, thoracic and mediastinal disorders / Hiccups / HICCUP	01AUG2018 (177)	14AUG2018 (190)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Abdominal discomfort / ABDOMEN DISCOMFORT	22MAY2018 (9)		Grade 2	Not Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Pruritus / SKIN ITCHING	29MAY2018 (16)	19JUN2018 (37)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Blood and lymphatic system disorders / Thrombocytopenia / THROMBOCYTOPENIA	04JUN2018 (22)	11JUN2018 (29)	Grade 3	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hyperuricaemia / HYPERURICEMIA	04JUN2018 (22)	11JUN2018 (29)	Grade 1	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE RENAL FAILURE	04JUN2018 (22)	19JUN2018 (37)	Grade 3	Resolved with Sequelae	Hospitalization/ Prolonged Hospitalization; Withdrawal from Study	Unrelated / Unrelated / Possibly / Not Applicable	Drug Withdrawn / Drug Withdrawn / Drug Withdrawn / Not Applicable	Yes
			Metabolism and nutrition disorders / Hyperkalaemia / HYPERKALEMIA	19JUN2018 (37)	30JUN2018 (48)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE RENAL FAILURE	19JUN2018 (37)	30JUN2018 (48)	Grade 2	Resolved	None	Unrelated / Unrelated / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0002	PlaceboPemPlatinum	Yes	Gastrointestinal disorders / Vomiting / VOMIT	20JUN2018 (38)	21JUN2018 (39)	Grade 1	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
			Infections and infestations / Sepsis / SEPSIS	30JUN2018 (48)	09JUL2018 (57)	Grade 5	Fatal	Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes
			Renal and urinary disorders / Acute kidney injury / ACUTE RENAL FAILURE	30JUN2018 (48)		Grade 3	Ongoing	None	Unrelated / Unrelated / Possibly / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	No
1206-0003	PlaceboPemPlatinum	Yes	Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	09APR2019 (9)	22APR2019 (22)	Grade 2	Resolved with Sequelae	Surgical/ Diagnostic Procedure	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Sepsis / SEPSIS	09APR2019 (9)	06MAY2019 (36)	Grade 3	Resolved	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	Yes
			Gastrointestinal disorders / Diarrhoea / DIARRHEA	09APR2019 (9)	08MAY2019 (38)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0003	PlaceboPemPlatinum	Yes	Nervous system disorders / Somnolence / CONSCIOUSNESS DROWSY	09APR2019 (9)	08MAY2019 (38)	Grade 2	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypoalbuminaemia / HYPOALBUMINEMIA	10APR2019 (10)	22APR2019 (22)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Investigations / Platelet count decreased / PLATELET COUNT DECREASE	12APR2019 (12)	22APR2019 (22)	Grade 3	Resolved	Surgical/ Diagnostic Procedure	Possibly / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Missing	No
			Gastrointestinal disorders / Upper gastrointestinal haemorrhage / UPPER GASTROINTESTINAL BLEEDING	14APR2019 (14)	08MAY2019 (38)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Metabolism and nutrition disorders / Hypernatraemia / HYPERNATREMIA	15APR2019 (15)	22APR2019 (22)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Cardiac disorders / Atrial fibrillation / PAROXYSMAL ATRIAL FIBRILLATION	15APR2019 (15)	08MAY2019 (38)	Grade 2	Resolved	None	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Skin and subcutaneous tissue disorders / Rash / SKIN RASH	16APR2019 (16)	08MAY2019 (38)	Grade 2	Resolved	Medication	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No

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^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death

Listing 16.2.7
Adverse Events

Subject ID	Treatment Group	Events Reported?	System Organ Class ^[1] / Preferred Term ^[1] / Event Name	Start Date (Study Day ^[2])	End Date (Study Day ^[2])	Severity Grade ^[3]	Outcome	Action Taken to Treat Event	Relationship to: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Action Taken with: ADI-PEG 20 or Placebo / Pemetrexed / Cisplatin / Carboplatin	Serious?
1206-0003	PlaceboPemPlatinum	Yes	Metabolism and nutrition disorders / Hypokalaemia / HYPOKALEMIA	22APR2019 (22)	25APR2019 (25)	Grade 3	Resolved	Medication	Possibly / Unlikely / Unlikely / Not Applicable	Drug Interrupted / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Renal and urinary disorders / Acute kidney injury / ACUTE KIDNEY INJURY	22APR2019 (22)	06MAY2019 (36)	Grade 1	Resolved	None	Unlikely / Possibly / Possibly / Not Applicable	Dose Not Changed / Drug Interrupted / Drug Interrupted / Not Applicable	No
			Blood and lymphatic system disorders / Anaemia / ANEMIA	22APR2019 (22)	08MAY2019 (38)	Grade 3	Resolved	Surgical/ Diagnostic Procedure	Unrelated / Unrelated / Unrelated / Not Applicable	Dose Not Changed / Dose Not Changed / Dose Not Changed / Not Applicable	No
			Infections and infestations / Septic shock / SEPTIC SHOCK	07MAY2019 (37)	08MAY2019 (38)	Grade 5	Fatal	Medication; Surgical/ Diagnostic Procedure; Hospitalization/ Prolonged Hospitalization	Unrelated / Unrelated / Unrelated / Not Applicable	Not Applicable / Not Applicable / Not Applicable / Not Applicable	Yes

^[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

^[2] Time (days) relative to date of first dose of study drug

^[3] Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death