Clinical trial results:
A Phase III Multicenter, Randomized, Open-Label Study Evaluating the Efficacy and Safety of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Carboplatin+Nab-Paclitaxel for Chemotherapy-Naive Patients With Stage IV Non-Squamous Non-Small Cell Lung Cancer

Summary

EudraCT number	2014-003206-32
Trial protocol	DE BE IT FR ES
Global end of trial date	18 January 2021

Results information

Result version number	v2
This version publication date	20 June 2021
First version publication date	29 March 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO29537

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02367781
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This randomized Phase III, multicenter, open-label study was designed to evaluate the safety and efficacy of atezolizumab (an engineered anti-programmed death-ligand 1 [PD-L1] antibody) in combination with carboplatin+nab-paclitaxel compared with treatment with carboplatin+nab-paclitaxel in chemotherapy-naive subjects with Stage IV non-squamous NSCLC.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	57 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 35
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Germany: 132
Country: Number of subjects enrolled	Spain: 71
Country: Number of subjects enrolled	France: 45
Country: Number of subjects enrolled	Italy: 52
Country: Number of subjects enrolled	Canada: 52
Country: Number of subjects enrolled	United States: 315
Worldwide total number of subjects	723
EEA total number of subjects	321

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	362
From 65 to 84 years	358
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

At the time of study completion a few participants that were still on maintenance treatment with atezolizumab were moved to another study, Post-Trial Access Program, or commercial use. Therefore, the reason for discontinuation was entered "Study terminated by Sponsor" for these participants.

Pre-assignment

Screening details:

Participants in this study included: histologically or cytologically confirmed, Stage IV non-squamous NSCLC; and no prior treatment for Stage IV non-squamous NSCLC.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)

Arm description:

Participants received intravenous (IV) infusion of atezolizumab and carboplatin on Day 1 of each 21-day cycle, and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurred first during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq, MPDL3280A, RO5541267
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at a dose of 1200 milligrams (mg) on Day 1 of each 21day cycle.

Investigational medicinal product name	Nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nab-paclitaxel was administered as IV infusion at a dose of 100 milligrams per square meter (mg/m^2) on Days 1, 8, and 15 of each 21-day cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered at area under the concentration curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle.

Arm title	Arm B (Nab-Paclitaxel+Carboplatin)

Arm description:

Participants received IV infusion of carboplatin on Day 1 and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression whichever occurs first during induction treatment phase. Participants received best supportive care during maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. Participants who were consented prior to approval of protocol Version 5 were given the option to cross over to receive atezolizumab as monotherapy until disease progression.

Arm type	Active comparator
Investigational medicinal product name	Nab-Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nab-paclitaxel was administered as IV infusion at a dose of 100 milligrams per square meter (mg/m^2) on Days 1, 8, and 15 of each 21-day cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered at area under the concentration curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Switch maintenance to pemetrexed can be administered within 6 weeks of Day 1 of the last induction cycle.

Number of subjects in period 1	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)
Started	483	240
Completed	0	0
Not completed	483	240
Adverse event, serious fatal	330	176
Physician decision	7	-
Immunotherapy Paused, Continuing Follow-Up Planned	1	-
Patient Admitted to Hospital	1	-
Patient Moving to Roll-Over Study	17	5
Study Terminated by Sponsor	3	1
Administrative-Change Facility	1	-
Death Prior First Dose	1	-

Prolonged Hospitalization	1	-
Consent withdrawn by subject	20	13
Non-Compliance	1	-
Sponsor Withdraw Patient in Survival Follow-Up	78	29
Sponsor Decision	2	-
Lost to follow-up	1	2
Patient Moved to Commercial Atezolizumab Use	14	9
Randomized in Error	5	4
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)
Reporting group description:	
Participants received intravenous (IV) infusion of atezolizumab and carboplatin on Day 1 of each 21-day cycle, and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurred first during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.	
Reporting group title	Arm B (Nab-Paclitaxel+Carboplatin)
Reporting group description:	
Participants received IV infusion of carboplatin on Day 1 and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression whichever occurs first during induction treatment phase. Participants received best supportive care during maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. Participants who were consented prior to approval of protocol Version 5 were given the option to cross over to receive atezolizumab as monotherapy until disease progression.	

Reporting group values	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)	Total
Number of subjects	483	240	723
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	245	117	362
From 65-84 years	236	122	358
85 years and over	2	1	3
Age Continuous Units: Years			
arithmetic mean	63.8	64.4	
standard deviation	± 9.5	± 8.9	-
Sex: Female, Male Units: Participants			
Female	206	102	308
Male	277	138	415
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	14	3	17
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	18	8	26
White	428	222	650
More than one race	2	0	2

Unknown or Not Reported	21	7	28
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	25	12	37
Not Hispanic or Latino	426	213	639
Unknown or Not Reported	32	15	47

End points

End points reporting groups

Reporting group title	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)

Reporting group description:

Participants received intravenous (IV) infusion of atezolizumab and carboplatin on Day 1 of each 21-day cycle, and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurred first during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Reporting group title	Arm B (Nab-Paclitaxel+Carboplatin)

Reporting group description:

Participants received IV infusion of carboplatin on Day 1 and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression whichever occurs first during induction treatment phase. Participants received best supportive care during maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. Participants who were consented prior to approval of protocol Version 5 were given the option to cross over to receive atezolizumab as monotherapy until disease progression.

Subject analysis set title	Arm B (Nab-Paclitaxel+Carboplatin Crossover)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of carboplatin on Day 1 and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression whichever occurred first during induction treatment phase. Participants received best supportive care during maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. Participants who were consented prior to approval of protocol Version 5 were given the option to cross over to receive atezolizumab as monotherapy until disease progression.

Primary: Progression-Free Survival (PFS) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the ITT-WT Population

End point title	Progression-Free Survival (PFS) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the ITT-WT Population

End point description:

PFS is defined as the time between the date of randomization and the date of first documented disease progression as determined by the investigator according to RECIST v1.1 or death from any cause, whichever occurs first in the ITT−WT population.

End point type	Primary

End point timeframe:

Up to approximately 35 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	456	229		
Units: Months				
median (confidence interval 95%)	7.0 (6.3 to 7.3)	5.5 (4.4 to 5.9)		

Statistical analyses

Statistical analysis title	PFS in ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	685
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.639
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.536
upper limit	0.763

Notes:

[1] - Stratified Analysis

Primary: Overall Survival (OS) in the ITT-WT Population

End point title	Overall Survival (OS) in the ITT-WT Population

End point description:

OS is defined as the time between the date of randomization and date of death from any cause in the ITT−WT population.

End point type	Primary

End point timeframe:

Up to approximately 35 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	456	229		
Units: Months				
median (confidence interval 95%)	18.6 (15.8 to 21.2)	13.9 (12.0 to 18.7)		

Statistical analyses

Statistical analysis title	OS in ITT-WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)

Number of subjects included in analysis	685
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0298
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.788
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.636
upper limit	0.977

Notes:

[2] - Stratified Analysis

Secondary: PFS as Determined by the Investigator Using Recist v1.1 in the ITT Population, PD-L1 Expression Population, and PD-L1 Expression WT Population

End point title	PFS as Determined by the Investigator Using Recist v1.1 in the ITT Population, PD-L1 Expression Population, and PD-L1 Expression WT Population

End point description:

PFS is defined as the time between the date of randomization and the date of first documented disease progression as determined by the investigator according to RECIST v1.1 or death from any cause, whichever occurs first. The ITT population was defined as all randomized participants, regardless of receipt of the assigned treatment. The PD-L1 expression population is defined as one of the following: PD-L1 IHC TC1/2/3 or IC1/2/3 population, defined as ITT participants with PD-L1 IHC TC1/2/3 or IC1/2/3 expression in baseline tumor tissue; PD-L1 IHC TC2/3 or IC2/3 population, defined as ITT participants with PD-L1 IHC TC2/3 or IC2/3 expression in baseline tumor tissue; PD-L1 IHC TC3 or IC3 population, defined as ITT participants with PD-L1 IHC TC3 or IC3 expression in baseline tumor tissue. The PD-L1 expression WT population is defined as the PD-L1 expression population excluding participants with an activating EGFR mutation or ALK translocation.

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	240		
Units: Months				
median (confidence interval 95%)				
ITT (n=483, n=240)	7.0 (6.3 to 7.3)	5.6 (4.5 to 5.9)		
TC1/2/3 or IC1/2/3 ITT (n=230, n=111)	7.5 (7.0 to 9.1)	5.7 (4.5 to 6.6)		
TC1/2/3 or IC1/2/3-WT ITT (n=216, n=107)	7.5 (7.0 to 9.0)	5.9 (4.5 to 6.6)		

Statistical analyses

Statistical analysis title	PFS in ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.647
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.545
upper limit	0.768

Notes:

[3] - Stratified Analysis

Statistical analysis title	PFS in TC1/2/3 or IC1/2/3-WT ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.561
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.432
upper limit	0.728

Notes:

[4] - Unstratified Analysis

Statistical analysis title	PFS in TC1/2/3 or IC1/2/3 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.549
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.425
upper limit	0.708

Notes:

[5] - Unstratified Analysis

Secondary: OS as Determined by the Investigator Using Recist v1.1 in the ITT Population

End point title	OS as Determined by the Investigator Using Recist v1.1 in the ITT Population

End point description:

OS is defined as the time between the date of randomization and date of death from any cause in the ITT population.

End point type	Secondary

End point timeframe:

Up to approximately 41 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	240		
Units: Months				
median (confidence interval 95%)	17.0 (14.9 to 19.7)	13.5 (11.9 to 17.7)		

Statistical analyses

Statistical analysis title	OS in ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.0732
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.837
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.689
upper limit	1.017

Notes:

[6] - Stratified Analysis

Secondary: OS as Determined by the Investigator Using RECIST v1.1 in the PD-L1 Expression Population and PD-L1 Expression WT Population

End point title	OS as Determined by the Investigator Using RECIST v1.1 in the

	PD-L1 Expression Population and PD-L1 Expression WT Population

End point description:

OS is defined as the time between the date of randomization and date of death from any cause in the PD-L1 Expression Population and PD-L1 Expression WT Population. The PD-L1 expression population is defined as one of the following: PD-L1 IHC TC1/2/3 or IC1/2/3 population, defined as ITT participants with PD-L1 IHC TC1/2/3 or IC1/2/3 expression in baseline tumor tissue; PD-L1 IHC TC2/3 or IC2/3 population, defined as ITT participants with PD-L1 IHC TC2/3 or IC2/3 expression in baseline tumor tissue; PD-L1 IHC TC3 or IC3 population, defined as ITT participants with PD-L1 IHC TC3 or IC3 expression in baseline tumor tissue. The PD-L1 expression WT population is defined as the PD-L1 expression population excluding participants with an activating EGFR mutation or ALK translocation.

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	111		
Units: Months				
median (confidence interval 95%)				
TC1/2/3 or IC1/2/3 ITT (n=230, n=111)	21.2 (17.3 to 28.2)	16.9 (12.5 to 22.0)		
TC1/2/3 or IC1/2/3 WT ITT (n=216, n=107)	21.2 (18.1 to 28.2)	16.9 (12.5 to 22.0)		

Statistical analyses

Statistical analysis title	OS in TC1/2/3 or IC1/2/3 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.083
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.752
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.545
upper limit	1.039

Notes:

[7] - Unstratified Analysis

Statistical analysis title	OS in TC1/2/3 or IC1/2/3 WT ITT Population

Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.0813
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.746
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.536
upper limit	1.038

Notes:

[8] - Unstratified Analysis

Secondary: Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using RECIST v1.1 in the ITT-WT Population

End point title	Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using RECIST v1.1 in the ITT-WT Population

End point description:

ORR (confirmation not required) is defined as the proportion of participants with an objective response, either CR or PR, with the use of RECIST v1.1, as determined by the investigator in the ITT-WT population.

End point type	Secondary

End point timeframe:

Up to approximately 41 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	452	227		
Units: Percentage of participants				
number (not applicable)	60.2	41.0		

Statistical analyses

Statistical analysis title	OR in ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)

Number of subjects included in analysis	679
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rate
Point estimate	19.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.05
upper limit	27.37

Notes:

[9] - Stratified Analysis

Secondary: Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using RECIST v1.1 in the ITT Population, PD-L1 Expression Population, and PD-L1 Expression WT Population

End point title	Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using RECIST v1.1 in the ITT Population, PD-L1 Expression Population, and PD-L1 Expression WT Population

End point description:

ORR (confirmation not required) is defined as proportion of participants with an objective response, either CR or PR, with the use of RECIST v1.1, as determined by investigator in ITT population, PD-L1 Expression population, and PD-L1 Expression WT population. ITT population was defined as all randomized participants, regardless of receipt of the assigned treatment. PD-L1 expression population is defined as one of the following: PD-L1 IHC TC1/2/3 or IC1/2/3 population, defined as ITT participants with PD-L1 IHC TC1/2/3 or IC1/2/3 expression in baseline tumor tissue; PD-L1 IHC TC2/3 or IC2/3 population, defined as ITT participants with PD-L1 IHC TC2/3 or IC2/3 expression in baseline tumor tissue; PD-L1 IHC TC3 or IC3 population, defined as ITT participants with PD-L1 IHC TC3 or IC3 expression in baseline tumor tissue. PD-L1 expression WT population is defined as PD-L1 expression population excluding participants with an activating EGFR mutation or ALK translocation.

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	479	237		
Units: Percentage of participants				
number (not applicable)				
ITT (n=479, n=237)	59.1	42.2		
TC1/2/3 or IC1/2/3 ITT WT (n=215, n=106)	65.6	46.2		
TC1/2/3 or IC1/2/3 ITT (n=229, n=109)	64.6	45.0		

Statistical analyses

Statistical analysis title	OR in ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rate
Point estimate	16.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.9
upper limit	24.88

Notes:

[10] - Stratified Analysis

Statistical analysis title	OR in TC1/2/3 or IC1/2/3 ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority[11]
Parameter estimate	Odds ratio (OR)
Point estimate	2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	3.56

Notes:

[11] - Stratified Analysis

Statistical analysis title	OR in TC1/2/3 or IC1/2/3 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)

Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.0007
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	3.51

Notes:

[12] - Stratified Analysis

Secondary: Duration of Response (DOR) as Determined by the Investigator Using RECIST v1.1 in ITT-WT Population, ITT Population, and PD-L1 Expression Population and PD-L1 Expression WT Population

End point title	Duration of Response (DOR) as Determined by the Investigator Using RECIST v1.1 in ITT-WT Population, ITT Population, and PD-L1 Expression Population and PD-L1 Expression WT Population

End point description:

DOR,defined for participants with objective response (OR) as time from 1st documented OR to documented disease progression as determined by investigator using RECIST v1.1,or death from any cause,whichever occurs 1st.ITT defined as all randomized participants,regardless of receipt of assigned treatment.ITT-WT defined as ITT population excluding participants with activating EGFR mutation or ALK translocation.PD-L1 expression population is defined as one of following:PD-L1 IHC TC1/2/3 or IC1/2/3 population,defined as ITT participants with PD-L1 IHC TC1/2/3 or IC1/2/3 expression in baseline tumor tissue;PD-L1 IHC TC2/3 or IC2/3 population, defined as ITT participants with PD-L1 IHC TC2/3 or IC2/3 expression in baseline tumor tissue;PD-L1 IHC TC3 or IC3 population,defined as ITT participants with PD-L1 IHC TC3 or IC3 expression in baseline tumor tissue.PD-L1 expression WT is defined as PD-L1 expression population excluding participants with activating EGFR mutation or ALK translocation.

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	100		
Units: Months				
median (confidence interval 95%)				
ITT (n=283, n=100)	6.2 (5.6 to 7.9)	5.4 (4.1 to 5.8)		
ITT-WT (n=267, n=93)	6.7 (5.6 to 8.0)	5.4 (3.9 to 5.8)		
TC1/2/3 or IC1/2/3 ITT (n=148, n=49)	7.2 (5.7 to 9.0)	5.0 (3.2 to 6.1)		
TC1/2/3 or IC1/2/3 ITT WT (n=141, n=49)	7.2 (5.7 to 9.0)	5.0 (3.2 to 6.1)		

Statistical analyses

Statistical analysis title	DOR in ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.0002
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.614
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.473
upper limit	0.797

Notes:

[13] - Unstratified Analysis

Statistical analysis title	DOR in ITT-WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.0002
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.458
upper limit	0.785

Notes:

[14] - Unstratified Analysis

Statistical analysis title	DOR in TC1/2/3 or IC1/2/3 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)

Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.0011
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.548
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.379
upper limit	0.791

Notes:

[15] - Unstratified Analysis

Statistical analysis title	DOR in TC1/2/3 or IC1/2/3 ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.0014
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.551
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.381
upper limit	0.798

Notes:

[16] - Unstratified Analysis

Secondary: Percentage of Participants Who are Alive at Year 1 and 2 in ITT-WT Population and ITT Population

End point title	Percentage of Participants Who are Alive at Year 1 and 2 in ITT-WT Population and ITT Population

End point description:

The OS rate at the 1- and 2-year landmark time points after randomization.

End point type	Secondary

End point timeframe:

Up to 41 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	240		
Units: Percentage of participants				
number (confidence interval 95%)				
Alive at Year 1 ITT WT	62.02 (57.53 to 66.51)	54.56 (48.04 to 61.08)		
Alive at Year 2 ITT WT	40.43 (35.64 to 45.22)	32.36 (25.80 to 38.92)		
Alive at Year 1 ITT	61.65 (57.29 to 66.02)	54.47 (48.09 to 60.84)		
Alive at Year 2 ITT	39.73 (35.10 to 44.37)	32.21 (25.79 to 38.63)		

Statistical analyses

Statistical analysis title	Alive at Year 1 ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0647
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	7.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	15.37

Statistical analysis title	Alive at Year 2 ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0516
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	8.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	16.19

Statistical analysis title	Alive at Year 1 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0683
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	7.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	14.91

Statistical analysis title	Alive at Year 2 ITT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0625
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	7.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	15.44

Secondary: Percentage of Participants Who are Alive at Year 1 and 2 in PD-L1 Expression Population and PD-L1 Expression WT Population

End point title	Percentage of Participants Who are Alive at Year 1 and 2 in PD-L1 Expression Population and PD-L1 Expression WT Population

End point description:

The OS rate at the 1- and 2-year landmark time points after randomization in the PD-L1 Expression Population and PD-L1 Expression WT Population. The PD-L1 expression population is defined as one of

the following: PD-L1 IHC TC1/2/3 or IC1/2/3 population, defined as ITT participants with PD-L1 IHC TC1/2/3 or IC1/2/3 expression in baseline tumor tissue; PD-L1 IHC TC2/3 or IC2/3 population, defined as ITT participants with PD-L1 IHC TC2/3 or IC2/3 expression in baseline tumor tissue; PD-L1 IHC TC3 or IC3 population, defined as ITT participants with PD-L1 IHC TC3 or IC3 expression in baseline tumor tissue. The PD-L1 expression WT population is defined as the PD-L1 expression population excluding participants with an activating EGFR mutation or ALK translocation.

End point type	Secondary

End point timeframe:

Up to 35 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	111		
Units: Percentage of participants				
number (confidence interval 95%)				
Year 1 TC1/2/3 or IC1/2/3 ITT (n=230, n=111)	68.56 (62.46 to 74.66)	61.86 (52.55 to 71.17)		
Year 2 TC1/2/3 or IC1/2/3 ITT(n=230, n=111)	44.63 (35.99 to 53.27)	35.98 (23.25 to 48.72)		
Year 1 TC1/2/3 or IC1/2/3 ITT WT (n=216, n=107)	68.84 (62.56 to 75.13)	62.51 (53.07 to 71.94)		
Year 2 TC1/2/3 or IC1/2/3 ITT WT (n=216, n=107)	44.02 (34.86 to 53.18)	35.33 (22.06 to 48.60)		

Statistical analyses

Statistical analysis title	Alive at Year 1 TC1/2/3 or IC1/2/3 ITT
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2385
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	6.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.44
upper limit	17.83

Statistical analysis title	Alive at Year 2 TC1/2/3 or IC1/2/3 ITT
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B

	(Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.271
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	8.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	24.03

Statistical analysis title	Alive at Year 1 TC1/2/3 or IC1/2/3 ITT WT
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2733
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	6.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	17.67

Statistical analysis title	Alive at Year 2 TC1/2/3 or IC1/2/3 ITT WT
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2909
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	8.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.44
upper limit	24.81

Secondary: Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms in the ITT-WT Population

End point title	Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms in the ITT-WT Population

End point description:

Defined as time from randomization to confirmed deterioration (10-point change) on the combined European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire−Core (EORTC QLQ-C30) and supplemental lung cancer module (EORTC QLQ-LC13) symptom subscales.

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	228		
Units: Months				
median (confidence interval 95%)	2.2 (1.8 to 3.1)	1.9 (1.5 to 2.4)		

Statistical analyses

Statistical analysis title	TTD in ITT WT Population
Comparison groups	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin) v Arm B (Nab-Paclitaxel+Carboplatin)
Number of subjects included in analysis	679
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.3342
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.893
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.711
upper limit	1.123

Notes:

[17] - Stratified Analysis

Secondary: Change From Baseline in Patient-Reported Lung Cancer Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale

End point title	Change From Baseline in Patient-Reported Lung Cancer

	Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale

End point description:

Change from baseline in patient-reported lung cancer symptoms (cough, dyspnea, and chest pain) on the symptom severity score of the Symptoms in Lung Cancer (SILC) scale. The SILC questionnaire comprises three individual symptoms (dyspnea, cough, chest pain) and will be scored at the individual symptom level, thus will have a dyspnea score, chest pain score, and cough score. Each individual symptom score will be calculated as the average of responses for the symptom items (e.g., Chest Pain Score = mean [item 1; item 2]). An increase in score is suggestive of a worsening in symptomology (i.e., frequency or severity). A score change of ≥ 0.3 points for the dyspnea and cough symptom scores is considered to be clinically significant; whereas a score change of ≥ 0.5 points for the chest pain score is considered to be clinically significant. Note: 999999=not available. FU=Follow-Up

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	129		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Chest Pain, Week 1 (n=203,n=114)	0.19 (± 0.86)	0.14 (± 0.90)		
Chest Pain, Week 2 (n=204,n=108)	-0.02 (± 0.89)	0.03 (± 0.91)		
Chest Pain, Week 3 (n=197,n=106)	-0.05 (± 0.95)	0.01 (± 0.92)		
Chest Pain, Week 4 (n=190,n=102)	-0.11 (± 0.95)	0.01 (± 1.02)		
Chest Pain, Week 5 (n=192,n=97)	-0.12 (± 0.99)	0.00 (± 1.03)		
Chest Pain, Week 6 (n=182,n=98)	-0.24 (± 1.07)	0.03 (± 1.03)		
Chest Pain, Week 7 (n=176,n=87)	-0.23 (± 1.11)	0.03 (± 1.08)		
Chest Pain, Week 8 (n=169,n=80)	-0.21 (± 0.99)	-0.14 (± 1.00)		
Chest Pain, Week 9 (n=172,n=80)	-0.18 (± 1.07)	-0.01 (± 1.07)		
Chest Pain, Week 10 (n=160,n=75)	-0.10 (± 1.07)	-0.07 (± 1.01)		
Chest Pain, Week 11 (n=171,n=78)	-0.11 (± 1.14)	0.01 (± 0.96)		
Chest Pain, Week 12 (n=160,n=72)	-0.15 (± 1.09)	-0.10 (± 1.13)		
Chest Pain, Week 13 (n=151,n=61)	-0.26 (± 1.07)	-0.03 (± 1.02)		
Chest Pain, Week 14 (n=144,n=62)	-0.28 (± 1.08)	-0.17 (± 1.18)		
Chest Pain, Week 15 (n=143,n=51)	-0.26 (± 1.14)	-0.19 (± 1.19)		
Chest Pain, Week 16 (n=139,n=52)	-0.33 (± 1.11)	-0.16 (± 1.20)		
Chest Pain, Week 17 (n=145,n=53)	-0.33 (± 1.11)	-0.14 (± 1.13)		
Chest Pain, Week 18 (n=136,n=49)	-0.28 (± 1.08)	-0.17 (± 1.13)		
Chest Pain, Week 19 (n=124,n=45)	-0.28 (± 1.04)	-0.16 (± 1.00)		
Chest Pain, Week 20 (n=123,n=43)	-0.26 (± 1.03)	-0.22 (± 1.02)		
Chest Pain, Week 21 (n=126,n=41)	-0.25 (± 1.04)	-0.32 (± 1.08)		
Chest Pain, Week 22 (n=116,n=37)	-0.28 (± 1.01)	-0.11 (± 1.03)		
Chest Pain, Week 23 (n=122,n=35)	-0.24 (± 1.03)	-0.19 (± 1.04)		
Chest Pain, Week 24 (n=110,n=34)	-0.21 (± 1.01)	-0.43 (± 1.03)		
Chest Pain, Week 25 (n=104,n=31)	-0.20 (± 0.98)	-0.24 (± 1.07)		
Chest Pain, Week 26 (n=109,n=31)	-0.17 (± 1.01)	-0.13 (± 0.91)		
Chest Pain, Week 27 (n=102,n=27)	-0.22 (± 1.01)	-0.15 (± 1.17)		

Chest Pain, Week 28 (n=96,n=28)	-0.20 (± 0.98)	-0.07 (± 0.91)		
Chest Pain, Week 29 (n=104,n=27)	-0.27 (± 1.09)	-0.04 (± 0.92)		
Chest Pain, Week 30 (n=100,n=23)	-0.15 (± 1.06)	-0.28 (± 1.12)		
Chest Pain, Week 31 (n=93,n=25)	-0.16 (± 0.95)	-0.12 (± 1.05)		
Chest Pain, Week 32 (n=88,n=25)	-0.19 (± 0.89)	-0.30 (± 1.10)		
Chest Pain, Week 33 (n=88,n=25)	-0.18 (± 1.00)	-0.18 (± 1.11)		
Chest Pain, Week 34 (n=85,n=24)	-0.18 (± 1.07)	-0.17 (± 1.18)		
Chest Pain, Week 35 (n=87,n=20)	-0.10 (± 1.09)	0.05 (± 1.06)		
Chest Pain, Week 36 (n=85,n=20)	-0.21 (± 1.08)	-0.35 (± 1.01)		
Chest Pain, Week 37 (n=82,n=21)	-0.18 (± 1.18)	-0.10 (± 1.04)		
Chest Pain, Week 38 (n=83,n=19)	-0.32 (± 1.02)	-0.05 (± 1.01)		
Chest Pain, Week 39 (n=78,n=18)	-0.28 (± 0.90)	-0.22 (± 1.06)		
Chest Pain, Week 40 (n=76,n=14)	-0.19 (± 0.87)	-0.39 (± 0.81)		
Chest Pain, Week 41 (n=77,n=16)	-0.25 (± 0.93)	-0.19 (± 0.89)		
Chest Pain, Week 42 (n=70,n=16)	-0.16 (± 1.02)	-0.41 (± 0.74)		
Chest Pain, Week 43 (n=68,n=16)	-0.24 (± 0.90)	-0.22 (± 0.95)		
Chest Pain, Week 44 (n=76,n=16)	-0.24 (± 0.95)	0.00 (± 0.98)		
Chest Pain, Week 45 (n=69,n=14)	-0.14 (± 0.95)	-0.07 (± 0.78)		
Chest Pain, Week 46 (n=71,n=15)	-0.15 (± 0.94)	-0.07 (± 1.03)		
Chest Pain, Week 47 (n=70,n=13)	-0.22 (± 0.98)	-0.15 (± 0.90)		
Chest Pain, Week 48 (n=66,n=11)	-0.14 (± 0.91)	-0.18 (± 0.98)		
Chest Pain, Week 49 (n=65,n=9)	-0.22 (± 0.91)	-0.72 (± 0.75)		
Chest Pain, Week 50 (n=70,n=8)	-0.18 (± 0.91)	-0.19 (± 0.70)		
Chest Pain, Week 51 (n=65,n=10)	-0.13 (± 0.71)	-0.50 (± 0.78)		
Chest Pain, Week 52 (n=72,n=7)	-0.15 (± 0.83)	-0.36 (± 0.63)		
Chest Pain, Week 53 (n=64,n=6)	-0.20 (± 0.82)	-0.33 (± 0.61)		
Chest Pain, Week 54 (n=65,n=7)	-0.22 (± 0.87)	-0.21 (± 0.70)		
Chest Pain, Week 55 (n=62,n=5)	-0.34 (± 0.80)	-0.30 (± 0.76)		
Chest Pain, Week 56 (n=62,n=6)	-0.19 (± 0.95)	-0.33 (± 0.68)		
Chest Pain, Week 57 (n=62,n=5)	-0.19 (± 0.76)	-0.40 (± 0.65)		
Chest Pain, Week 58 (n=56,n=4)	-0.32 (± 0.92)	-0.50 (± 1.15)		
Chest Pain, Week 59 (n=52,n=4)	-0.25 (± 0.93)	-0.63 (± 0.75)		
Chest Pain, Week 60 (n=48,n=4)	-0.27 (± 1.03)	-0.50 (± 1.08)		
Chest Pain, Week 61 (n=49,n=5)	-0.28 (± 1.02)	-0.20 (± 1.15)		
Chest Pain, Week 62 (n=41,n=5)	-0.16 (± 1.06)	-0.40 (± 1.47)		
Chest Pain, Week 63 (n=43,n=5)	-0.12 (± 0.82)	-0.10 (± 1.34)		
Chest Pain, Week 64 (n=42,n=4)	-0.15 (± 0.83)	0.38 (± 1.44)		
Chest Pain, Week 65 (n=40,n=3)	-0.31 (± 0.84)	0.17 (± 1.76)		
Chest Pain, Week 66 (n=38,n=4)	-0.25 (± 0.92)	0.25 (± 1.19)		
Chest Pain, Week 67 (n=33,n=4)	-0.18 (± 0.86)	0.13 (± 1.44)		
Chest Pain, Week 68 (n=34,n=4)	-0.15 (± 0.93)	-0.25 (± 1.55)		
Chest Pain, Week 69 (n=35,n=3)	-0.13 (± 0.83)	-0.17 (± 1.89)		
Chest Pain, Week 70 (n=36,n=3)	-0.14 (± 0.93)	0.00 (± 1.80)		
Chest Pain, Week 71 (n=31,n=3)	-0.10 (± 0.88)	0.00 (± 0.87)		
Chest Pain, Week 72 (n=29,n=2)	-0.24 (± 0.85)	-1.00 (± 0.71)		
Chest Pain, Week 73 (n=28,n=1)	-0.25 (± 1.02)	-1.50 (± 999999)		
Chest Pain, Week 74 (n=31,n=1)	-0.08 (± 0.93)	-1.50 (± 999999)		
Chest Pain, Week 75 (n=31,n=1)	-0.21 (± 0.98)	-1.50 (± 999999)		
Chest Pain, Week 76 (n=29,n=1)	0.03 (± 1.00)	-1.50 (± 999999)		

Chest Pain, Week 77 (n=26,n=2)	-0.06 (± 0.89)	-1.50 (± 0.00)		
Chest Pain, Week 78 (n=23,n=1)	-0.04 (± 0.84)	-1.50 (± 999999)		
Chest Pain, Week 79 (n=19,n=1)	-0.11 (± 1.09)	-0.50 (± 999999)		
Chest Pain, Week 80 (n=20,n=1)	-0.18 (± 1.05)	-1.50 (± 999999)		
Chest Pain, Week 81 (n=17,n=1)	-0.59 (± 0.96)	-1.50 (± 999999)		
Chest Pain, Week 82 (n=18,n=1)	-0.39 (± 0.96)	-1.50 (± 999999)		
Chest Pain, Week 83 (n=22,n=1)	-0.34 (± 0.90)	-1.50 (± 999999)		
Chest Pain, Week 84 (n=20,n=1)	-0.20 (± 0.75)	-1.50 (± 999999)		
Chest Pain, Week 85 (n=17,n=1)	-0.44 (± 0.97)	-1.50 (± 999999)		
Chest Pain, Week 86 (n=12,n=1)	-0.38 (± 0.64)	-1.50 (± 999999)		
Chest Pain, Week 87 (n=15,n=1)	-0.53 (± 1.01)	-1.50 (± 999999)		
Chest Pain, Week 88 (n=14,n=1)	-0.46 (± 1.06)	-1.50 (± 999999)		
Chest Pain, Week 89 (n=11,n=1)	-0.55 (± 0.96)	-1.50 (± 999999)		
Chest Pain, Week 90 (n=14,n=1)	-0.18 (± 0.85)	-1.50 (± 999999)		
Chest Pain, Week 91 (n=11,n=1)	-0.32 (± 1.08)	-1.50 (± 999999)		
Chest Pain, Week 92 (n=10,n=1)	-0.40 (± 0.66)	-1.50 (± 999999)		
Chest Pain, Week 93 (n=11,n=1)	-0.18 (± 1.08)	-1.50 (± 999999)		
Chest Pain, Week 94 (n=10,n=1)	-0.30 (± 1.09)	999999 (± 999999)		
Chest Pain, Week 95 (n=10,n=0)	-0.05 (± 1.26)	999999 (± 999999)		
Chest Pain, Week 96 (n=9,n=0)	-0.17 (± 1.25)	999999 (± 999999)		
Chest Pain, Week 97 (n=8,n=0)	-0.19 (± 1.31)	999999 (± 999999)		
Chest Pain, Week 98 (n=10,n=0)	-0.25 (± 1.16)	999999 (± 999999)		
Chest Pain, Week 99 (n=7,n=0)	-0.21 (± 1.47)	999999 (± 999999)		
Chest Pain, Week 100 (n=6,n=0)	-0.50 (± 1.38)	999999 (± 999999)		
Chest Pain, Week 101 (n=7,n=0)	-0.36 (± 1.38)	999999 (± 999999)		
Chest Pain, Week 102 (n=4,n=0)	-0.75 (± 1.71)	999999 (± 999999)		
Chest Pain, Week 103 (n=6,n=0)	-0.33 (± 1.54)	999999 (± 999999)		
Chest Pain, Week 104 (n=5,n=0)	-0.60 (± 1.39)	999999 (± 999999)		
Chest Pain, Week 105 (n=4,n=0)	-1.00 (± 1.41)	999999 (± 999999)		
Chest Pain, Week 106 (n=4,n=0)	-1.00 (± 1.41)	999999 (± 999999)		
Chest Pain, Week 107 (n=4,n=0)	-1.00 (± 1.41)	999999 (± 999999)		

Chest Pain, Week 108 (n=4,n=0)	-0.75 (± 1.50)	999999 (± 999999)		
Chest Pain, Week 109 (n=5,n=0)	-0.60 (± 1.52)	999999 (± 999999)		
Chest Pain, Week 110 (n=6,n=0)	-0.42 (± 1.43)	999999 (± 999999)		
Chest Pain, Week 111 (n=5,n=0)	-0.50 (± 1.50)	999999 (± 999999)		
Chest Pain, Week 112 (n=4,n=0)	-0.13 (± 0.63)	999999 (± 999999)		
Chest Pain, Week 113 (n=4,n=0)	0.13 (± 0.63)	999999 (± 999999)		
Chest Pain, Week 114 (n=3,n=0)	0.00 (± 1.00)	999999 (± 999999)		
Chest Pain, Week 115 (n=2,n=0)	0.25 (± 0.35)	999999 (± 999999)		
Chest Pain, Week 116 (n=2,n=0)	0.50 (± 0.71)	999999 (± 999999)		
Chest Pain, Week 117 (n=2,n=0)	0.25 (± 1.06)	999999 (± 999999)		
Chest Pain, Week 118 (n=2,n=0)	-0.25 (± 1.06)	999999 (± 999999)		
Chest Pain, Week 119 (n=2,n=0)	-0.25 (± 0.35)	999999 (± 999999)		
Chest Pain, Week 120 (n=2,n=0)	0.00 (± 0.71)	999999 (± 999999)		
Chest Pain, Week 121 (n=2,n=0)	0.00 (± 1.41)	999999 (± 999999)		
Chest Pain, Week 122 (n=2,n=0)	0.00 (± 1.41)	999999 (± 999999)		
Chest Pain, Week 123 (n=2,n=0)	-0.75 (± 1.77)	999999 (± 999999)		
Chest Pain, Week 124 (n=1,n=0)	0.50 (± 999999)	999999 (± 999999)		
Chest Pain, Week 125 (n=1,n=0)	0.50 (± 999999)	999999 (± 999999)		
Chest Pain, Survival FU Month 1 (n=158, n=58)	0.01 (± 1.13)	0.22 (± 0.87)		
Chest Pain, Survival FU Month 2 (n=42, n=47)	-0.07 (± 1.18)	-0.16 (± 0.96)		
Chest Pain, Survival FU Month 3 (n=36, n=26)	0.15 (± 1.33)	-0.08 (± 0.87)		
Chest Pain, Survival FU Month 4 (n=23, n=28)	-0.28 (± 1.40)	-0.07 (± 0.79)		
Chest Pain, Survival FU Month 5 (n=22, n=22)	-0.11 (± 1.49)	-0.02 (± 0.65)		
Chest Pain, Survival FU Month 6 (n=15, n=21)	-0.37 (± 1.67)	0.02 (± 0.78)		
Cough, Week 1 (n=203, n=114)	0.08 (± 0.69)	0.04 (± 0.73)		
Cough, Week 2 (n=204, n=108)	0.02 (± 0.78)	0.04 (± 0.84)		
Cough, Week 3 (n=197, n=106)	0.02 (± 0.86)	-0.09 (± 0.93)		
Cough, Week 4 (n=190, n=102)	-0.06 (± 0.86)	-0.10 (± 0.93)		
Cough, Week 5 (n=192, n=97)	-0.09 (± 0.84)	-0.09 (± 0.99)		
Cough, Week 6 (n=182, n=98)	-0.15 (± 0.86)	-0.08 (± 0.98)		
Cough, Week 7 (n=176, n=87)	-0.11 (± 0.86)	-0.06 (± 1.01)		
Cough, Week 8 (n=169, n=80)	-0.13 (± 0.95)	-0.21 (± 1.04)		
Cough, Week 9 (n=172, n=80)	-0.15 (± 0.99)	-0.13 (± 1.23)		
Cough, Week 10 (n=166, n=75)	-0.20 (± 1.05)	-0.07 (± 1.17)		
Cough, Week 11 (n=171, n=78)	-0.15 (± 1.03)	-0.15 (± 1.17)		
Cough, Week 12 (n=160, n=72)	-0.17 (± 1.03)	-0.11 (± 1.09)		

Cough, Week 13 (n=151, n=61)	-0.24 (± 1.08)	-0.04 (± 1.11)		
Cough, Week 14 (n=144, n=62)	-0.23 (± 1.06)	-0.18 (± 1.08)		
Cough, Week 15 (n=143, n=51)	-0.27 (± 1.06)	-0.05 (± 1.10)		
Cough, Week 16 (n=139, n=52)	-0.37 (± 1.07)	-0.25 (± 1.09)		
Cough, Week 17 (n=145, n=53)	-0.32 (± 1.09)	-0.21 (± 1.01)		
Cough, Week 18 (n=136, n=49)	-0.33 (± 1.07)	-0.33 (± 1.09)		
Cough, Week 19 (n=124, n=45)	-0.33 (± 1.06)	-0.40 (± 0.89)		
Cough, Week 20 (n=123, n=43)	-0.37 (± 1.10)	-0.31 (± 0.90)		
Cough, Week 21 (n=126, n=41)	-0.37 (± 1.08)	-0.33 (± 0.96)		
Cough, Week 22 (n=116, n=37)	-0.37 (± 1.15)	-0.24 (± 0.97)		
Cough, Week 23 (n=122, n=35)	-0.30 (± 1.10)	-0.41 (± 1.03)		
Cough, Week 24 (n=110, n=34)	-0.38 (± 1.09)	-0.54 (± 1.04)		
Cough, Week 25 (n=104, n=31)	-0.49 (± 0.91)	-0.47 (± 1.05)		
Cough, Week 26 (n=109, n=31)	-0.43 (± 0.99)	-0.34 (± 1.02)		
Cough, Week 27 (n=102, n=27)	-0.41 (± 0.97)	-0.48 (± 0.98)		
Cough, Week 28 (n=96, n=28)	-0.52 (± 0.96)	-0.43 (± 0.84)		
Cough, Week 29 (n=104, n=27)	-0.43 (± 0.98)	-0.46 (± 0.91)		
Cough, Week 30 (n=100, n=23)	-0.43 (± 0.95)	-0.46 (± 1.07)		
Cough, Week 31 (n=93, n=25)	-0.32 (± 1.07)	-0.38 (± 0.77)		
Cough, Week 32 (n=88, n=25)	-0.30 (± 0.94)	-0.12 (± 0.99)		
Cough, Week 33 (n=88, n=25)	-0.19 (± 1.12)	-0.52 (± 1.03)		
Cough, Week 34 (n=85, n=24)	-0.35 (± 1.12)	-0.33 (± 1.03)		
Cough, Week 35 (n=87, n=20)	-0.46 (± 1.01)	0.00 (± 1.22)		
Cough, Week 36 (n=85, n=20)	-0.35 (± 1.08)	-0.20 (± 1.01)		
Cough, Week 37 (n=82, n=21)	-0.46 (± 1.03)	-0.45 (± 1.11)		
Cough, Week 38 (n=83, n=19)	-0.38 (± 1.06)	-0.03 (± 0.89)		
Cough, Week 39 (n=78, n=18)	-0.27 (± 0.99)	-0.17 (± 1.00)		
Cough, Week 40 (n=76, n=14)	-0.38 (± 0.95)	-0.50 (± 0.90)		
Cough, Week 41 (n=77, n=16)	-0.44 (± 0.92)	-0.22 (± 0.77)		
Cough, Week 42 (n=70, n=16)	-0.44 (± 0.92)	-0.41 (± 0.97)		
Cough, Week 43 (n=68, n=16)	-0.39 (± 0.98)	-0.13 (± 0.92)		
Cough, Week 44 (n=76, n=16)	-0.38 (± 0.94)	-0.16 (± 0.89)		
Cough, Week 45 (n=69, n=14)	-0.30 (± 1.10)	-0.14 (± 1.03)		
Cough, Week 46 (n=71, n=15)	-0.25 (± 0.99)	-0.03 (± 1.23)		
Cough, Week 47 (n=70, n=13)	-0.44 (± 0.88)	-0.12 (± 1.23)		
Cough, Week 48 (n=66, n=11)	-0.29 (± 0.99)	0.14 (± 1.21)		
Cough, Week 49 (n=65, n=9)	-0.38 (± 1.00)	-0.56 (± 1.36)		
Cough, Week 50 (n=70, n=8)	-0.39 (± 0.96)	-0.19 (± 1.16)		
Cough, Week 51 (n=65, n=10)	-0.30 (± 1.00)	-0.40 (± 1.20)		
Cough, Week 52 (n=72, n=7)	-0.32 (± 1.03)	-0.21 (± 1.07)		
Cough, Week 53 (n=64, n=6)	-0.37 (± 1.03)	-0.17 (± 1.33)		
Cough, Week 54 (n=65, n=7)	-0.41 (± 0.93)	-0.07 (± 1.21)		
Cough, Week 55 (n=62, n=5)	-0.40 (± 0.93)	0.10 (± 1.34)		
Cough, Week 56 (n=62, n=6)	-0.26 (± 0.94)	0.17 (± 1.13)		
Cough, Week 57 (n=62, n=5)	-0.35 (± 0.98)	0.00 (± 1.27)		
Cough, Week 58 (n=56, n=4)	-0.33 (± 1.06)	0.13 (± 1.31)		
Cough, Week 59 (n=52, n=4)	-0.31 (± 0.97)	0.13 (± 1.60)		
Cough, Week 60 (n=48, n=4)	-0.42 (± 0.89)	0.38 (± 1.18)		
Cough, Week 61 (n=49, n=5)	-0.35 (± 0.95)	0.80 (± 1.20)		
Cough, Week 62 (n=41, n=5)	-0.23 (± 1.03)	0.50 (± 1.62)		
Cough, Week 63 (n=43, n=5)	-0.22 (± 1.04)	0.50 (± 1.27)		
Cough, Week 64 (n=42, n=4)	-0.19 (± 1.07)	0.00 (± 1.87)		

Cough, Week 65 (n=40, n=3)	-0.23 (± 1.04)	0.83 (± 1.04)		
Cough, Week 66 (n=38, n=4)	-0.29 (± 0.90)	0.63 (± 1.03)		
Cough, Week 67 (n=33, n=4)	-0.48 (± 0.91)	0.38 (± 1.38)		
Cough, Week 68 (n=34, n=4)	-0.34 (± 0.82)	0.13 (± 1.49)		
Cough, Week 69 (n=35, n=3)	-0.34 (± 1.03)	0.17 (± 1.61)		
Cough, Week 70 (n=36, n=3)	-0.26 (± 0.94)	0.17 (± 1.61)		
Cough, Week 71 (n=31, n=3)	-0.23 (± 0.91)	0.33 (± 1.04)		
Cough, Week 72 (n=29, n=2)	-0.48 (± 0.87)	-1.50 (± 1.41)		
Cough, Week 73 (n=28, n=1)	-0.43 (± 0.91)	-0.50 (± 999999)		
Cough, Week 74 (n=31, n=1)	-0.42 (± 0.93)	-0.50 (± 999999)		
Cough, Week 75 (n=31, n=1)	-0.32 (± 1.00)	-0.50 (± 999999)		
Cough, Week 76 (n=29, n=1)	-0.31 (± 0.91)	-0.50 (± 999999)		
Cough, Week 77 (n=26, n=2)	-0.40 (± 0.92)	-0.50 (± 2.83)		
Cough, Week 78 (n=23, n=1)	-0.52 (± 0.94)	0.00 (± 999999)		
Cough, Week 79 (n=19, n=1)	-0.08 (± 0.93)	1.00 (± 999999)		
Cough, Week 80 (n=20, n=1)	-0.48 (± 0.87)	1.00 (± 999999)		
Cough, Week 81 (n=17, n=1)	-0.44 (± 1.01)	-0.50 (± 999999)		
Cough, Week 82 (n=18, n=1)	-0.39 (± 0.90)	1.00 (± 999999)		
Cough, Week 83 (n=22, n=1)	-0.25 (± 1.09)	0.50 (± 999999)		
Cough, Week 84 (n=20, n=1)	-0.30 (± 0.91)	1.00 (± 999999)		
Cough, Week 85 (n=17, n=1)	-0.32 (± 1.25)	1.50 (± 999999)		
Cough, Week 86 (n=12, n=1)	-0.54 (± 1.27)	0.00 (± 999999)		
Cough, Week 87 (n=15, n=1)	-0.33 (± 1.18)	0.00 (± 999999)		
Cough, Week 88 (n=14, n=1)	-0.46 (± 1.26)	0.00 (± 999999)		
Cough, Week 89 (n=11, n=1)	-0.36 (± 1.07)	0.00 (± 999999)		
Cough, Week 90 (n=14, n=1)	-0.29 (± 1.05)	0.00 (± 999999)		
Cough, Week 91 (n=11, n=1)	-0.27 (± 1.17)	0.00 (± 999999)		
Cough, Week 92 (n=10, n=1)	-0.35 (± 1.27)	1.00 (± 999999)		
Cough, Week 93 (n=11, n=1)	-0.55 (± 0.96)	0.00 (± 999999)		
Cough, Week 94 (n=10, n=0)	-0.40 (± 0.81)	999999 (± 999999)		
Cough, Week 95 (n=10, n=0)	0.05 (± 1.23)	999999 (± 999999)		
Cough, Week 96 (n=9, n=0)	-0.28 (± 1.28)	999999 (± 999999)		
Cough, Week 97 (n=8, n=0)	-0.31 (± 1.19)	999999 (± 999999)		
Cough, Week 98 (n=10, n=0)	-0.10 (± 0.99)	999999 (± 999999)		

Cough, Week 99 (n=7, n=0)	-0.43 (± 0.98)	999999 (± 999999)		
Cough, Week 100 (n=6, n=0)	-0.58 (± 0.86)	999999 (± 999999)		
Cough, Week 101 (n=7, n=0)	-0.50 (± 0.96)	999999 (± 999999)		
Cough, Week 102 (n=4, n=0)	-0.50 (± 0.41)	999999 (± 999999)		
Cough, Week 103 (n=6, n=0)	-0.75 (± 0.42)	999999 (± 999999)		
Cough, Week 104 (n=5, n=0)	-0.80 (± 0.27)	999999 (± 999999)		
Cough, Week 105 (n=4, n=0)	-0.63 (± 0.48)	999999 (± 999999)		
Cough, Week 106 (n=4, n=0)	-0.63 (± 0.48)	999999 (± 999999)		
Cough, Week 107 (n=4, n=0)	-0.63 (± 0.48)	999999 (± 999999)		
Cough, Week 108 (n=4, n=0)	-0.50 (± 0.71)	999999 (± 999999)		
Cough, Week 109 (n=5, n=0)	-0.50 (± 0.50)	999999 (± 999999)		
Cough, Week 110 (n=6, n=0)	-0.50 (± 0.45)	999999 (± 999999)		
Cough, Week 111 (n=5, n=0)	-0.30 (± 0.84)	999999 (± 999999)		
Cough, Week 112 (n=4, n=0)	-0.63 (± 0.48)	999999 (± 999999)		
Cough, Week 113 (n=4, n=0)	-0.25 (± 0.65)	999999 (± 999999)		
Cough, Week 114 (n=3, n=0)	-0.33 (± 0.29)	999999 (± 999999)		
Cough, Week 115 (n=2, n=0)	0.25 (± 0.35)	999999 (± 999999)		
Cough, Week 116 (n=2, n=0)	-0.25 (± 1.06)	999999 (± 999999)		
Cough, Week 117 (n=2, n=0)	-0.50 (± 0.71)	999999 (± 999999)		
Cough, Week 118 (n=2, n=0)	-0.25 (± 0.35)	999999 (± 999999)		
Cough, Week 119 (n=2, n=0)	0.00 (± 0.00)	999999 (± 999999)		
Cough, Week 120 (n=2, n=0)	-0.25 (± 0.35)	999999 (± 999999)		
Cough, Week 121 (n=2, n=0)	-0.50 (± 0.71)	999999 (± 999999)		
Cough, Week 122 (n=2, n=0)	-0.50 (± 0.71)	999999 (± 999999)		
Cough, Week 123 (n=2, n=0)	-0.75 (± 1.06)	999999 (± 999999)		
Cough, Week 124 (n=1, n=0)	0.50 (± 999999)	999999 (± 999999)		
Cough, Week 125 (n=1, n=0)	0.50 (± 999999)	999999 (± 999999)		
Cough, Survival Follow-Up Month 1 (n=158, n=58)	-0.21 (± 1.05)	-0.01 (± 0.96)		
Cough, Survival Follow-Up Month 2 (n=42, n=47)	-0.07 (± 1.16)	-0.31 (± 1.18)		
Cough, Survival Follow-Up Month 3 (n=36, n=26)	-0.14 (± 1.12)	-0.13 (± 1.32)		
Cough, Survival Follow-Up Month 4 (n=23, n=28)	-0.39 (± 1.15)	-0.45 (± 1.17)		

Cough, Survival Follow-Up Month 5 (n=22, n=22)	-0.25 (± 1.44)	-0.27 (± 1.32)		
Cough, Survival Follow-Up Month 6 (n=15, n=21)	-0.23 (± 1.53)	-0.29 (± 1.26)		
Dyspnoea, Week 1 (n=203, n=114)	0.13 (± 0.76)	0.23 (± 0.79)		
Dyspnoea, Week 2 (n=204, n=108)	0.10 (± 0.68)	0.31 (± 0.84)		
Dyspnoea, Week 3 (n=197, n=106)	0.22 (± 0.78)	0.32 (± 0.76)		
Dyspnoea, Week 4 (n=190, n=102)	0.23 (± 0.80)	0.45 (± 0.84)		
Dyspnoea, Week 5 (n=192, n=97)	0.26 (± 0.84)	0.42 (± 0.92)		
Dyspnoea, Week 6 (n=182, n=96)	0.27 (± 0.92)	0.51 (± 0.95)		
Dyspnoea, Week 7 (n=176, n=87)	0.29 (± 0.88)	0.60 (± 1.00)		
Dyspnoea, Week 8 (n=169, n=80)	0.32 (± 0.97)	0.53 (± 1.02)		
Dyspnoea, Week 9 (n=172, n=80)	0.38 (± 0.95)	0.62 (± 1.07)		
Dyspnoea, Week 10 (n=166, n=75)	0.41 (± 1.04)	0.75 (± 1.13)		
Dyspnoea, Week 11 (n=171, n=78)	0.50 (± 1.05)	0.60 (± 1.06)		
Dyspnoea, Week 12 (n=160, n=72)	0.47 (± 1.07)	0.74 (± 1.08)		
Dyspnoea, Week 13 (n=151, n=61)	0.32 (± 1.00)	0.76 (± 1.00)		
Dyspnoea, Week 14 (n=144, n=62)	0.34 (± 0.99)	0.61 (± 1.10)		
Dyspnoea, Week 15 (n=143, n=51)	0.29 (± 1.06)	0.71 (± 1.02)		
Dyspnoea, Week 16 (n=139, n=52)	0.22 (± 0.99)	0.67 (± 1.11)		
Dyspnoea, Week 17 (n=145, n=53)	0.28 (± 1.10)	0.68 (± 1.03)		
Dyspnoea, Week 18 (n=136, n=49)	0.23 (± 1.02)	0.62 (± 1.03)		
Dyspnoea, Week 19 (n=124, n=45)	0.26 (± 1.06)	0.54 (± 0.95)		
Dyspnoea, Week 20 (n=123, n=43)	0.24 (± 1.02)	0.54 (± 1.08)		
Dyspnoea, Week 21 (n=126, n=41)	0.26 (± 1.04)	0.39 (± 1.05)		
Dyspnoea, Week 22 (n=116, n=37)	0.21 (± 0.94)	0.41 (± 1.05)		
Dyspnoea, Week 23 (n=122, n=35)	0.18 (± 0.97)	0.41 (± 1.06)		
Dyspnoea, Week 24 (n=110, n=34)	0.22 (± 0.93)	0.31 (± 1.01)		
Dyspnoea, Week 25 (n=104, n=31)	0.21 (± 0.88)	0.20 (± 0.91)		
Dyspnoea, Week 26 (n=109, n=31)	0.17 (± 0.89)	0.30 (± 1.00)		
Dyspnoea, Week 27 (n=102, n=27)	0.20 (± 1.04)	0.30 (± 0.92)		
Dyspnoea, Week 28 (n=96, n=28)	0.16 (± 0.94)	0.22 (± 1.01)		
Dyspnoea, Week 29 (n=104, n=27)	0.16 (± 0.92)	0.33 (± 0.98)		
Dyspnoea, Week 30 (n=100, n=23)	0.24 (± 1.04)	0.27 (± 1.02)		
Dyspnoea, Week 31 (n=93, n=25)	0.12 (± 0.99)	0.26 (± 1.04)		
Dyspnoea, Week 32 (n=88, n=25)	0.20 (± 0.95)	0.38 (± 1.06)		
Dyspnoea, Week 33 (n=88, n=25)	0.18 (± 0.98)	0.19 (± 1.14)		
Dyspnoea, Week 34 (n=85, n=24)	0.21 (± 1.06)	0.30 (± 1.02)		
Dyspnoea, Week 35 (n=87, n=20)	0.22 (± 1.03)	0.46 (± 0.96)		
Dyspnoea, Week 36 (n=85, n=20)	0.21 (± 1.09)	0.34 (± 1.14)		
Dyspnoea, Week 37 (n=82, n=21)	0.16 (± 1.13)	0.10 (± 1.07)		
Dyspnoea, Week 38 (n=83, n=19)	0.18 (± 1.07)	0.51 (± 0.99)		
Dyspnoea, Week 39 (n=78, n=18)	0.31 (± 1.04)	0.26 (± 0.83)		
Dyspnoea, Week 40 (n=76, n=14)	0.31 (± 0.99)	0.04 (± 0.79)		
Dyspnoea, Week 41 (n=77, n=16)	0.24 (± 0.99)	0.18 (± 0.85)		
Dyspnoea, Week 42 (n=70, n=16)	0.26 (± 1.03)	0.08 (± 0.70)		
Dyspnoea, Week 43 (n=68, n=16)	0.17 (± 1.13)	0.41 (± 0.91)		
Dyspnoea, Week 44 (n=76, n=16)	0.22 (± 1.06)	0.29 (± 0.86)		
Dyspnoea, Week 45 (n=69, n=14)	0.26 (± 1.09)	0.31 (± 0.90)		
Dyspnoea, Week 46 (n=71, n=15)	0.29 (± 0.99)	0.47 (± 1.03)		
Dyspnoea, Week 47 (n=70, n=13)	0.20 (± 1.02)	0.45 (± 0.85)		
Dyspnoea, Week 48 (n=66, n=11)	0.32 (± 1.00)	0.29 (± 0.91)		

Dyspnoea, Week 49 (n=65, n=9)	0.24 (± 1.04)	0.00 (± 1.30)		
Dyspnoea, Week 50 (n=70, n=8)	0.32 (± 0.98)	0.43 (± 0.88)		
Dyspnoea, Week 51 (n=65, n=10)	0.24 (± 0.92)	0.06 (± 1.04)		
Dyspnoea, Week 52 (n=72, n=7)	0.27 (± 0.95)	0.29 (± 0.90)		
Dyspnoea, Week 53 (n=64, n=6)	0.24 (± 1.00)	0.30 (± 0.85)		
Dyspnoea, Week 54 (n=65, n=7)	0.28 (± 0.89)	0.40 (± 0.95)		
Dyspnoea, Week 55 (n=62, n=5)	0.26 (± 0.98)	0.44 (± 1.02)		
Dyspnoea, Week 56 (n=62, n=6)	0.26 (± 0.97)	0.53 (± 1.10)		
Dyspnoea, Week 57 (n=62, n=5)	0.37 (± 0.95)	0.24 (± 1.08)		
Dyspnoea, Week 58 (n=56, n=4)	0.19 (± 1.01)	0.35 (± 1.40)		
Dyspnoea, Week 59 (n=52, n=4)	0.32 (± 0.84)	0.35 (± 1.40)		
Dyspnoea, Week 60 (n=48, n=4)	0.35 (± 0.99)	0.50 (± 1.51)		
Dyspnoea, Week 61 (n=49, n=5)	0.33 (± 1.03)	0.60 (± 1.40)		
Dyspnoea, Week 62 (n=41, n=5)	0.45 (± 0.99)	0.72 (± 1.36)		
Dyspnoea, Week 63 (n=43, n=5)	0.44 (± 1.05)	0.56 (± 1.35)		
Dyspnoea, Week 64 (n=42, n=4)	0.36 (± 0.98)	-0.50 (± 1.91)		
Dyspnoea, Week 65 (n=40, n=3)	0.27 (± 0.97)	0.07 (± 1.68)		
Dyspnoea, Week 66 (n=38, n=4)	0.32 (± 1.11)	0.50 (± 1.23)		
Dyspnoea, Week 67 (n=33, n=4)	0.28 (± 0.91)	0.40 (± 1.36)		
Dyspnoea, Week 68 (n=34, n=4)	0.35 (± 0.96)	0.40 (± 1.43)		
Dyspnoea, Week 69 (n=35, n=3)	0.44 (± 1.02)	0.73 (± 1.55)		
Dyspnoea, Week 70 (n=36, n=3)	0.33 (± 0.97)	0.73 (± 1.55)		
Dyspnoea, Week 71 (n=31, n=3)	0.50 (± 0.95)	0.60 (± 1.51)		
Dyspnoea, Week 72 (n=29, n=3)	0.17 (± 0.95)	0.60 (± 1.44)		
Dyspnoea, Week 73 (n=28, n=2)	0.41 (± 0.96)	-1.80 (± 1.13)		
Dyspnoea, Week 74 (n=31, n=1)	0.30 (± 1.00)	-1.00 (± 999999)		
Dyspnoea, Week 75 (n=31, n=1)	0.26 (± 0.89)	-1.00 (± 999999)		
Dyspnoea, Week 76 (n=29, n=1)	0.23 (± 0.89)	-1.00 (± 999999)		
Dyspnoea, Week 77 (n=26, n=2)	0.20 (± 0.97)	-1.50 (± 1.56)		
Dyspnoea, Week 78 (n=23, n=1)	0.31 (± 0.94)	-1.00 (± 999999)		
Dyspnoea, Week 79 (n=19, n=1)	0.32 (± 0.95)	-1.00 (± 999999)		
Dyspnoea, Week 80 (n=20, n=1)	0.30 (± 0.92)	-1.00 (± 999999)		
Dyspnoea, Week 81 (n=17, n=1)	-0.12 (± 1.00)	-0.80 (± 999999)		
Dyspnoea, Week 82 (n=18, n=1)	0.02 (± 1.06)	-0.80 (± 999999)		
Dyspnoea, Week 83 (n=22, n=1)	0.13 (± 1.01)	-1.00 (± 999999)		
Dyspnoea, Week 84 (n=20, n=1)	0.19 (± 1.00)	-1.00 (± 999999)		
Dyspnoea, Week 85 (n=17, n=1)	0.05 (± 1.17)	-0.80 (± 999999)		
Dyspnoea, Week 86 (n=12, n=1)	-0.07 (± 1.05)	-1.00 (± 999999)		
Dyspnoea, Week 87 (n=15, n=1)	-0.11 (± 0.96)	-1.00 (± 999999)		
Dyspnoea, Week 88 (n=14, n=1)	0.06 (± 1.12)	-1.00 (± 999999)		
Dyspnoea, Week 89 (n=11, n=1)	0.09 (± 0.91)	-1.00 (± 999999)		

Dyspnoea, Week 90 (n=14, n=1)	0.37 (± 0.83)	-1.00 (± 999999)		
Dyspnoea, Week 91 (n=11, n=1)	0.33 (± 1.11)	-1.00 (± 999999)		
Dyspnoea, Week 92 (n=10, n=1)	0.20 (± 1.05)	-0.80 (± 999999)		
Dyspnoea, Week 93 (n=93, n=1)	0.35 (± 0.96)	-0.80 (± 999999)		
Dyspnoea, Week 94 (n=10, n=0)	0.50 (± 0.93)	999999 (± 999999)		
Dyspnoea, Week 95 (n=10, n=0)	0.48 (± 0.98)	999999 (± 999999)		
Dyspnoea, Week 96 (n=9, n=0)	0.51 (± 1.09)	999999 (± 999999)		
Dyspnoea, Week 97 (n=8, n=0)	0.33 (± 1.18)	999999 (± 999999)		
Dyspnoea, Week 98 (n=10, n=0)	0.38 (± 1.05)	999999 (± 999999)		
Dyspnoea, Week 99 (n=7, n=0)	0.11 (± 0.99)	999999 (± 999999)		
Dyspnoea, Week 100 (n=6, n=0)	0.27 (± 1.11)	999999 (± 999999)		
Dyspnoea, Week 101 (n=7, n=0)	0.20 (± 1.11)	999999 (± 999999)		
Dyspnoea, Week 102 (n=4, n=0)	0.35 (± 1.06)	999999 (± 999999)		
Dyspnoea, Week 103 (n=6, n=0)	0.47 (± 1.29)	999999 (± 999999)		
Dyspnoea, Week 104 (n=5, n=0)	0.48 (± 1.22)	999999 (± 999999)		
Dyspnoea, Week 105 (n=4, n=0)	-0.20 (± 0.71)	999999 (± 999999)		
Dyspnoea, Week 106 (n=4, n=0)	-0.20 (± 0.99)	999999 (± 999999)		
Dyspnoea, Week 107 (n=4, n=0)	-0.30 (± 0.62)	999999 (± 999999)		
Dyspnoea, Week 108 (n=4, n=0)	-0.15 (± 0.98)	999999 (± 999999)		
Dyspnoea, Week 109 (n=5, n=0)	0.16 (± 1.17)	999999 (± 999999)		
Dyspnoea, Week 110 (n=6, n=0)	0.33 (± 1.00)	999999 (± 999999)		
Dyspnoea, Week 111 (n=5, n=0)	-0.04 (± 0.86)	999999 (± 999999)		
Dyspnoea, Week 112 (n=4, n=0)	0.20 (± 0.43)	999999 (± 999999)		
Dyspnoea, Week 113 (n=4, n=0)	0.20 (± 0.67)	999999 (± 999999)		
Dyspnoea, Week 114 (n=3, n=0)	0.40 (± 0.72)	999999999999 (± 999999)		
Dyspnoea, Week 115 (n=2, n=0)	0.80 (± 0.85)	999999 (± 999999)		
Dyspnoea, Week 116 (n=2, n=0)	0.60 (± 0.57)	999999 (± 999999)		
Dyspnoea, Week 117 (n=2, n=0)	0.30 (± 0.14)	999999 (± 999999)		
Dyspnoea, Week 118 (n=2, n=0)	0.30 (± 0.42)	999999 (± 999999)		
Dyspnoea, Week 119 (n=2, n=0)	0.50 (± 0.42)	999999 (± 999999)		
Dyspnoea, Week 120 (n=2, n=0)	0.30 (± 0.42)	999999 (± 999999)		

Dyspnoea, Week 121 (n=2, n=0)	0.60 (± 0.57)	999999 (± 999999)		
Dyspnoea, Week 122 (n=2, n=0)	0.60 (± 0.00)	999999 (± 999999)		
Dyspnoea, Week 123 (n=2, n=0)	-0.20 (± 0.57)	999999 (± 999999)		
Dyspnoea, Week 124 (n=1, n=0)	-0.20 (± 999999)	999999 (± 999999)		
Dyspnoea, Week 125 (n=1, n=0)	0.20 (± 999999)	999999 (± 999999)		
Dyspnoea, Survival Follow-Up Month 1 (n=158, n=58)	0.41 (± 1.11)	0.60 (± 1.14)		
Dyspnoea, Survival Follow-Up Month 2 (n=42, n=47)	0.36 (± 1.20)	0.46 (± 1.22)		
Dyspnoea, Survival Follow-Up Month 3 (n=36, n=26)	0.27 (± 0.96)	0.61 (± 1.19)		
Dyspnoea, Survival Follow-Up Month 4 (n=23, n=28)	0.02 (± 1.11)	0.45 (± 0.88)		
Dyspnoea, Survival Follow-Up Month 5 (n=22, n=22)	0.13 (± 1.24)	0.48 (± 1.00)		
Dyspnoea, Survival Follow-Up Month 6 (n=15, n=21)	-0.09 (± 1.29)	0.54 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

Percentage of participants with at least one adverse event. Adverse event onset date before cross over.

End point type	Secondary

End point timeframe:

Up to approximately 69 months after first patient enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	473	232		
Units: Percentage of participants				
number (not applicable)	99.6	98.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab

End point title	Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab

End point description:

Baseline prevalence and post-baseline incidence of anti-drug antibodies (ADA) to Atezolizumab in the Arm A (Atezolizumab + Carboplatin or Cisplatin + Pemetrexed) and Arm B Carboplatin+nab-paclitaxel Crossover Participants

End point type	Secondary

End point timeframe:

Up to approximately 35 months after first subject enrolled

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)	Arm B (Nab-Paclitaxel+Carboplatin)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	85		
Units: Perecentage of participants				
number (not applicable)				
Baseline (n=451, n=84)	3.1	4.8		
Post-baseline (n=446, n=85)	22.4	23.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab for Patients in Atezolizumab+Carboplatin+Nab-Paclitaxel Arm

End point title	Maximum Observed Serum Concentration (Cmax) of Atezolizumab for Patients in Atezolizumab+Carboplatin+Nab-Paclitaxel Arm[18]

End point description:

Predose samples will be collected on the same day of treatment administration. The infusion duration of atezolizumab will be of 30-60 minutes.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 3 Day 1 (Cycle length = 21 days)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)			
Subject group type	Reporting group			
Number of subjects analysed	465			
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=446)	392 (± 114)			
Cycle 3 Day 1 (n=356)	454 (± 170)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Atezolizumab+Carboplain+Nab-Paclitaxel

End point title	Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Atezolizumab+Carboplain+Nab-Paclitaxel[19]

End point description:

Predose samples will be collected on the same day of treatment administration.

End point type	Secondary

End point timeframe:

Cycle 1 Day 21, Cycle 2 Day 21, Cycle 3 Day 21, and Cycle 7 Day 21 (Cycle length = 21 days)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)			
Subject group type	Reporting group			
Number of subjects analysed	465			
Units: mcg/mL				
geometric mean (standard deviation)				
Cycle 1 Day 21 (n=416)	70.9 (± 35.1)			
Cycle 2 Day 21 (n=384)	111 (± 52.2)			
Cycle 3 Day 21 (n=352)	134 (± 57.8)			
Cycle 7 Day 21 (n=257)	218 (± 93.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Carboplatin for Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)

End point title	Plasma Concentrations of Carboplatin for Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)[20]

End point description:

Note: 999999=non-reportable.

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of carboplatin infusion, 1 hour after carboplatin infusion (infusion duration=15 to 30 minutes) on Day 1 of Cycle 1 and 3 (1 Cycle=21 days) (up to approximately 35 months)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Pre-dose (n=29)	999999 (± 999999)			
Cycle 1 Day 1 Before End of Infusion (n=23)	20500 (± 7500)			
Cycle 1 Day 1 Post Infusion(n=29)	11900 (± 3100)			
Cycle 3 Day 1 Pre-dose (n=23)	169 (± 63.8)			
Cycle 3 Day 1 Before End of Infusion (n=16)	15300 (± 6600)			
Cycle 3 Day 1 Post Infusion (n=18)	11400 (± 3060)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Carboplatin for Arm B (Nab-Paclitaxel+Carboplatin CrossOver)

End point title	Plasma Concentrations of Carboplatin for Arm B (Nab-Paclitaxel+Carboplatin CrossOver)

End point description:

Note: 999999=non-reportable.

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of carboplatin infusion, 1 hour after carboplatin infusion (infusion duration=15 to 30 minutes) on Day 1 of Cycle 1 and 3 (1 Cycle=21 days) (up to approximately 35 months)

End point values	Arm B (Nab-Paclitaxel+Carboplatin Crossover)			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (Pre-dose) (n=19)	999999 (± 999999)			
Cycle 1 Day 1 Before End of Infusion (n=18)	17000 (± 5200)			
Cycle 1 Day 1 Post Infusion (n=18)	12400 (± 3800)			
Cycle 3 Day 1 Pre-dose (n=16)	160 (± 48.8)			
Cycle 3 Day 1 Before End of Infusion (n=14)	17800 (± 7550)			
Cycle 3 Day 1 Post Infusion (n=15)	13400 (± 6650)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Nab-Paclitaxel Reported as Total Paclitaxel for Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)

End point title	Plasma Concentrations of Nab-Paclitaxel Reported as Total Paclitaxel for Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)[21]

End point description:

Note: 999999=non-reportable.

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of nab-paclitaxel infusion, 1 hour after nab-paclitaxel infusion (infusion duration=30 minutes) on Day 1 of Cycle 1 and 3 (1 Cycle=21 days) (up to approximately 35 months)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Arm A (Atezolizumab +Nab-Paclitaxel+Carboplatin)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: ng/mL				
arithmetic mean (standard deviation)				

Cycle 1 Day 1 Pre-dose (n=29)	999999 (± 999999)			
Cycle 1 Day 1 Before End of Infusion (n=27)	3520 (± 2210)			
Cycle 1 Day 1 Post Infusion (n=25)	307 (± 153)			
Cycle 3 Day 1 Pre-dose (n=23)	999999 (± 999999)			
Cycle 3 Day 1 Before End of Infusion (n=17)	4480 (± 3520)			
Cycle 3 Day 1 Post Infusion (n=18)	357 (± 253)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Nab-Paclitaxel Reported as Total Paclitaxel for Arm B (Nab-Paclitaxel+Carboplatin Crossover)

End point title	Plasma Concentrations of Nab-Paclitaxel Reported as Total Paclitaxel for Arm B (Nab-Paclitaxel+Carboplatin Crossover)

End point description:

Note: 999999=non-reportable.

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of nab-paclitaxel infusion, 1 hour after nab-paclitaxel infusion (infusion duration=30 minutes) on Day 1 of Cycle 1 and 3 (1 Cycle=21 days) (up to approximately 35 months)

End point values	Arm B (Nab-Paclitaxel+Carboplatin Crossover)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Pre-dose (n=19)	999999 (± 999999)			
Cycle 1 Day 1 Before End of Infusion (n=15)	2530 (± 1420)			
Cycle 1 Day 1 Post Infusion (n=17)	417 (± 217)			
Cycle 3 Day 1 Pre-dose (n=16)	999999 (± 999999)			
Cycle 3 Day 1 Before End of Infusion (n=10)	2030 (± 1690)			
Cycle 3 Day 1 Post Infusion (n=15)	447 (± 322)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug to the data cutoff date: 18 January 2021 (approximately 69 months)

Adverse event reporting additional description:

Safety-evaluable population included all treated participants, defined as randomized participants who received any protocol treatment. For safety analyses, participants were grouped according to whether any full or partial dose of atezolizumab was received, including when atezolizumab was received in error.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Arm B (Nab-Paclitaxel+Carboplatin)

Reporting group description:

Participants received IV infusion of carboplatin on Day 1 and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression whichever occurs first during induction treatment phase. Participants received best supportive care during maintenance treatment phase. Switch maintenance to pemetrexed was also permitted. Participants who were consented prior to approval of protocol Version 5 were given the option to cross over to receive atezolizumab as monotherapy until disease progression.

Reporting group title	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)

Reporting group description:

Participants received intravenous (IV) infusion of atezolizumab and carboplatin on Day 1 of each 21-day cycle, and nab-paclitaxel on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurred first during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Serious adverse events	Arm B (Nab-Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)	
Total subjects affected by serious adverse events			
subjects affected / exposed	87 / 232 (37.50%)	252 / 473 (53.28%)	
number of deaths (all causes)	178	338	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR PAIN			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADENOCARCINOMA OF COLON			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-SMALL CELL LUNG CANCER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SARCOMA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	2 / 232 (0.86%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMBOLISM			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMORAL ARTERY ANEURYSM			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
JUGULAR VEIN THROMBOSIS			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHLEBITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR STENOSIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	0 / 232 (0.00%)	5 / 473 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	3 / 232 (1.29%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 3	1 / 1	
DRUG INTERACTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

FATIGUE			
subjects affected / exposed	2 / 232 (0.86%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	2 / 232 (0.86%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	2 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUCOSAL INFLAMMATION			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERFORMANCE STATUS DECREASED			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			

subjects affected / exposed	2 / 232 (0.86%)	8 / 473 (1.69%)	
occurrences causally related to treatment / all	1 / 2	5 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPIRATION			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ASTHMA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	5 / 232 (2.16%)	13 / 473 (2.75%)	
occurrences causally related to treatment / all	1 / 8	0 / 22	
deaths causally related to treatment / all	0 / 2	0 / 1	
COUGH			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	1 / 232 (0.43%)	12 / 473 (2.54%)	
occurrences causally related to treatment / all	0 / 1	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPTYSIS			
subjects affected / exposed	3 / 232 (1.29%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 2	
LUNG DISORDER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANISING PNEUMONIA			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OROPHARYNGEAL DISCOMFORT			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 232 (0.00%)	8 / 473 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	3 / 232 (1.29%)	9 / 473 (1.90%)	
occurrences causally related to treatment / all	1 / 3	9 / 9	
deaths causally related to treatment / all	0 / 1	2 / 2	
PNEUMOTHORAX			
subjects affected / exposed	2 / 232 (0.86%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX SPONTANEOUS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	5 / 232 (2.16%)	17 / 473 (3.59%)	
occurrences causally related to treatment / all	1 / 5	0 / 18	
deaths causally related to treatment / all	0 / 1	0 / 6	
PULMONARY HAEMORRHAGE			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISTRESS			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
RESPIRATORY FAILURE			
subjects affected / exposed	2 / 232 (0.86%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISORIENTATION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 232 (0.00%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 232 (0.00%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 232 (0.00%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

LIPASE INCREASED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL FRACTURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC FRACTURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA UNSTABLE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 232 (0.43%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRADYCARDIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ANEURYSM			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			

subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
CARDIAC FAILURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 232 (0.43%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	1 / 3	
PALPITATIONS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 232 (0.00%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
ACUTE CORONARY SYNDROME			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
ATAXIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAROTID ARTERY STENOSIS			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	2 / 232 (0.86%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMBOLIC STROKE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			

subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LETHARGY			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARAESTHESIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	1 / 232 (0.43%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOXIC NEUROPATHY			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASOGENIC CEREBRAL OEDEMA			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
AGRANULOCYTOSIS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	8 / 232 (3.45%)	14 / 473 (2.96%)	
occurrences causally related to treatment / all	6 / 8	12 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	5 / 232 (2.16%)	9 / 473 (1.90%)	
occurrences causally related to treatment / all	5 / 5	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOLYTIC URAEMIC SYNDROME			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			

subjects affected / exposed	2 / 232 (0.86%)	14 / 473 (2.96%)	
occurrences causally related to treatment / all	2 / 2	16 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 232 (0.00%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			

subjects affected / exposed	1 / 232 (0.43%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	2 / 232 (0.86%)	14 / 473 (2.96%)	
occurrences causally related to treatment / all	1 / 2	12 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL VASCULAR MALFORMATION HAEMORRHAGIC			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS PARALYTIC			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINAL STENOSIS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MELAENA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	4 / 232 (1.72%)	5 / 473 (1.06%)	
occurrences causally related to treatment / all	3 / 5	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL FOOD IMPACTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	2 / 232 (0.86%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			

subjects affected / exposed	4 / 232 (1.72%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	3 / 5	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE-MEDIATED ENTEROCOLITIS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
AUTOIMMUNE HEPATITIS			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BILE DUCT STONE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLESTASIS			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC CIRRHOSIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
HEPATITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATOCELLULAR INJURY			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE-MEDIATED HEPATITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DRUG ERUPTION			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN ULCER			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 232 (0.00%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHRITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROLITHIASIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROPATHY TOXIC			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTRENAL FAILURE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	2 / 232 (0.86%)	5 / 473 (1.06%)	
occurrences causally related to treatment / all	1 / 2	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUBULOINTERSTITIAL NEPHRITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AUTOIMMUNE NEPHRITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ADDISON'S DISEASE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GLUCOCORTICOID DEFICIENCY			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE PAIN			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYALGIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL PAIN			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR SPINAL STENOSIS			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATYPICAL PNEUMONIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERIAL COLITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERIAL SEPSIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 232 (0.43%)	6 / 473 (1.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONJUNCTIVITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYSTITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE INFECTION			

subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GANGRENE			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	1 / 232 (0.43%)	2 / 473 (0.42%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIOUS PLEURAL EFFUSION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	1 / 232 (0.43%)	5 / 473 (1.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASOPHARYNGITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC INFECTION			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	15 / 232 (6.47%)	45 / 473 (9.51%)	
occurrences causally related to treatment / all	3 / 17	12 / 55	
deaths causally related to treatment / all	0 / 2	0 / 5	
PULMONARY SEPSIS			

subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 232 (0.43%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	2 / 232 (0.86%)	7 / 473 (1.48%)	
occurrences causally related to treatment / all	1 / 2	1 / 7	
deaths causally related to treatment / all	1 / 2	0 / 1	
SEPTIC SHOCK			
subjects affected / exposed	2 / 232 (0.86%)	5 / 473 (1.06%)	
occurrences causally related to treatment / all	0 / 2	3 / 5	
deaths causally related to treatment / all	0 / 1	1 / 1	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
TRACHEOBRONCHITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 232 (0.43%)	4 / 473 (0.85%)	
occurrences causally related to treatment / all	1 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOMEGALOVIRUS COLITIS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FURUNCLE			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARAPHARYNGEAL SPACE INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH INFECTION			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			

subjects affected / exposed	2 / 232 (0.86%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	2 / 232 (0.86%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETES MELLITUS			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETIC KETOACIDOSIS			
subjects affected / exposed	1 / 232 (0.43%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERKALAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOCALCAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			

subjects affected / exposed	2 / 232 (0.86%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	1 / 2	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	1 / 473 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	0 / 232 (0.00%)	3 / 473 (0.63%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	1 / 232 (0.43%)	0 / 473 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm B (Nab-Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Nab-Paclitaxel+Carboplatin)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	227 / 232 (97.84%)	467 / 473 (98.73%)	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	13 / 232 (5.60%)	34 / 473 (7.19%)	
occurrences (all)	15	43	
HYPERTENSION			
subjects affected / exposed	8 / 232 (3.45%)	26 / 473 (5.50%)	
occurrences (all)	10	33	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	40 / 232 (17.24%)	89 / 473 (18.82%)	
occurrences (all)	55	133	
CHEST PAIN			

subjects affected / exposed	12 / 232 (5.17%)	33 / 473 (6.98%)	
occurrences (all)	12	43	
FATIGUE			
subjects affected / exposed	109 / 232 (46.98%)	228 / 473 (48.20%)	
occurrences (all)	134	297	
OEDEMA PERIPHERAL			
subjects affected / exposed	25 / 232 (10.78%)	71 / 473 (15.01%)	
occurrences (all)	30	81	
PAIN			
subjects affected / exposed	8 / 232 (3.45%)	30 / 473 (6.34%)	
occurrences (all)	10	33	
PYREXIA			
subjects affected / exposed	22 / 232 (9.48%)	80 / 473 (16.91%)	
occurrences (all)	31	104	
CHILLS			
subjects affected / exposed	7 / 232 (3.02%)	25 / 473 (5.29%)	
occurrences (all)	8	32	
MUCOSAL INFLAMMATION			
subjects affected / exposed	8 / 232 (3.45%)	24 / 473 (5.07%)	
occurrences (all)	9	26	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	39 / 232 (16.81%)	135 / 473 (28.54%)	
occurrences (all)	42	162	
DYSPNOEA			
subjects affected / exposed	51 / 232 (21.98%)	134 / 473 (28.33%)	
occurrences (all)	59	181	
EPISTAXIS			
subjects affected / exposed	27 / 232 (11.64%)	69 / 473 (14.59%)	
occurrences (all)	30	84	
HAEMOPTYSIS			
subjects affected / exposed	8 / 232 (3.45%)	30 / 473 (6.34%)	
occurrences (all)	8	42	
PRODUCTIVE COUGH			

subjects affected / exposed	8 / 232 (3.45%)	35 / 473 (7.40%)	
occurrences (all)	8	44	
PNEUMONITIS			
subjects affected / exposed	0 / 232 (0.00%)	24 / 473 (5.07%)	
occurrences (all)	0	26	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	7 / 232 (3.02%)	32 / 473 (6.77%)	
occurrences (all)	7	32	
DEPRESSION			
subjects affected / exposed	5 / 232 (2.16%)	29 / 473 (6.13%)	
occurrences (all)	5	29	
INSOMNIA			
subjects affected / exposed	31 / 232 (13.36%)	70 / 473 (14.80%)	
occurrences (all)	33	76	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	14 / 232 (6.03%)	26 / 473 (5.50%)	
occurrences (all)	18	42	
BLOOD CREATININE INCREASED			
subjects affected / exposed	8 / 232 (3.45%)	27 / 473 (5.71%)	
occurrences (all)	13	32	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	35 / 232 (15.09%)	93 / 473 (19.66%)	
occurrences (all)	62	188	
PLATELET COUNT DECREASED			
subjects affected / exposed	38 / 232 (16.38%)	108 / 473 (22.83%)	
occurrences (all)	61	179	
WEIGHT DECREASED			
subjects affected / exposed	28 / 232 (12.07%)	63 / 473 (13.32%)	
occurrences (all)	29	71	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	18 / 232 (7.76%)	49 / 473 (10.36%)	
occurrences (all)	28	80	
Injury, poisoning and procedural complications			

FALL			
subjects affected / exposed	4 / 232 (1.72%)	24 / 473 (5.07%)	
occurrences (all)	4	33	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	25 / 232 (10.78%)	78 / 473 (16.49%)	
occurrences (all)	36	90	
DYSGEUSIA			
subjects affected / exposed	12 / 232 (5.17%)	43 / 473 (9.09%)	
occurrences (all)	12	46	
HEADACHE			
subjects affected / exposed	23 / 232 (9.91%)	85 / 473 (17.97%)	
occurrences (all)	26	106	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	22 / 232 (9.48%)	56 / 473 (11.84%)	
occurrences (all)	26	58	
PARAESTHESIA			
subjects affected / exposed	12 / 232 (5.17%)	43 / 473 (9.09%)	
occurrences (all)	13	51	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	23 / 232 (9.91%)	60 / 473 (12.68%)	
occurrences (all)	29	71	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	117 / 232 (50.43%)	259 / 473 (54.76%)	
occurrences (all)	134	357	
LEUKOPENIA			
subjects affected / exposed	19 / 232 (8.19%)	51 / 473 (10.78%)	
occurrences (all)	29	92	
NEUTROPENIA			
subjects affected / exposed	105 / 232 (45.26%)	213 / 473 (45.03%)	
occurrences (all)	194	424	
THROMBOCYTOPENIA			
subjects affected / exposed	60 / 232 (25.86%)	132 / 473 (27.91%)	
occurrences (all)	96	210	
Eye disorders			

VISION BLURRED			
subjects affected / exposed	6 / 232 (2.59%)	25 / 473 (5.29%)	
occurrences (all)	6	28	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	17 / 232 (7.33%)	54 / 473 (11.42%)	
occurrences (all)	20	67	
CONSTIPATION			
subjects affected / exposed	71 / 232 (30.60%)	176 / 473 (37.21%)	
occurrences (all)	89	224	
DIARRHOEA			
subjects affected / exposed	72 / 232 (31.03%)	196 / 473 (41.44%)	
occurrences (all)	102	321	
DYSPEPSIA			
subjects affected / exposed	7 / 232 (3.02%)	33 / 473 (6.98%)	
occurrences (all)	8	34	
NAUSEA			
subjects affected / exposed	105 / 232 (45.26%)	236 / 473 (49.89%)	
occurrences (all)	150	354	
STOMATITIS			
subjects affected / exposed	12 / 232 (5.17%)	40 / 473 (8.46%)	
occurrences (all)	14	45	
VOMITING			
subjects affected / exposed	43 / 232 (18.53%)	130 / 473 (27.48%)	
occurrences (all)	68	228	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	11 / 232 (4.74%)	25 / 473 (5.29%)	
occurrences (all)	14	33	
DRY MOUTH			
subjects affected / exposed	5 / 232 (2.16%)	24 / 473 (5.07%)	
occurrences (all)	5	24	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	6 / 232 (2.59%)	24 / 473 (5.07%)	
occurrences (all)	7	25	
Skin and subcutaneous tissue disorders			

ALOPECIA			
subjects affected / exposed	63 / 232 (27.16%)	152 / 473 (32.14%)	
occurrences (all)	63	155	
DRY SKIN			
subjects affected / exposed	12 / 232 (5.17%)	28 / 473 (5.92%)	
occurrences (all)	12	31	
PRURITUS			
subjects affected / exposed	12 / 232 (5.17%)	61 / 473 (12.90%)	
occurrences (all)	12	81	
RASH			
subjects affected / exposed	17 / 232 (7.33%)	73 / 473 (15.43%)	
occurrences (all)	19	86	
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	1 / 232 (0.43%)	51 / 473 (10.78%)	
occurrences (all)	1	55	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	36 / 232 (15.52%)	113 / 473 (23.89%)	
occurrences (all)	40	161	
BACK PAIN			
subjects affected / exposed	16 / 232 (6.90%)	89 / 473 (18.82%)	
occurrences (all)	16	105	
MUSCULAR WEAKNESS			
subjects affected / exposed	14 / 232 (6.03%)	25 / 473 (5.29%)	
occurrences (all)	16	27	
MYALGIA			
subjects affected / exposed	10 / 232 (4.31%)	50 / 473 (10.57%)	
occurrences (all)	12	60	
PAIN IN EXTREMITY			
subjects affected / exposed	15 / 232 (6.47%)	61 / 473 (12.90%)	
occurrences (all)	15	72	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	6 / 232 (2.59%)	29 / 473 (6.13%)	
occurrences (all)	7	30	

NASOPHARYNGITIS			
subjects affected / exposed	10 / 232 (4.31%)	38 / 473 (8.03%)	
occurrences (all)	11	61	
PNEUMONIA			
subjects affected / exposed	8 / 232 (3.45%)	37 / 473 (7.82%)	
occurrences (all)	8	41	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	12 / 232 (5.17%)	35 / 473 (7.40%)	
occurrences (all)	15	55	
URINARY TRACT INFECTION			
subjects affected / exposed	19 / 232 (8.19%)	63 / 473 (13.32%)	
occurrences (all)	20	91	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	64 / 232 (27.59%)	144 / 473 (30.44%)	
occurrences (all)	70	169	
DEHYDRATION			
subjects affected / exposed	25 / 232 (10.78%)	52 / 473 (10.99%)	
occurrences (all)	35	73	
HYPOKALAEMIA			
subjects affected / exposed	24 / 232 (10.34%)	77 / 473 (16.28%)	
occurrences (all)	29	98	
HYPOMAGNESAEMIA			
subjects affected / exposed	40 / 232 (17.24%)	94 / 473 (19.87%)	
occurrences (all)	50	130	
HYPONATRAEMIA			
subjects affected / exposed	8 / 232 (3.45%)	31 / 473 (6.55%)	
occurrences (all)	10	54	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2015	Protocol was amended to include change to the name of the test product from MPDL3280A to atezolizumab. The evaluations of progression-free survival at 6 months and at 1 year and overall survival at 3 years have been added as exploratory objectives to further evaluate the clinical benefit of atezolizumab at these time points. The contraception requirements in the inclusion and exclusion criteria and the pregnancy-reporting information have been updated to be consistent with safety information for nab-paclitaxel. The study inclusion criteria have been modified, on the basis of data from an expanding safety database, to allow for patients with treated, asymptomatic cerebellar metastases to be enrolled provided specific criteria are met. The exclusion criteria for history of autoimmune disease has been broadened, on the basis of data from an expanding safety database, to allow for patients with eczema, psoriasis, or lichen simplex chronicus of vitiligo with dermatologic manifestations only to be permitted provided that they meet the specific conditions. The study exclusion criterion regarding treatment with systemic immunostimulatory agents within 6 weeks or 5 half-lives of the drug (whichever is shorter) prior to randomization has been modified to 4 weeks prior to randomization for consistency with more recent atezolizumab protocols. The exclusion criterion specifying that patients with a history of allergic reaction to intravenous contrast that requires steroid pretreatment should have baseline and subsequent tumor assessments performed via magnetic resonance imaging (MRI) has been removed because this is in conflict with Section 4.5.5. Patients with contraindications to contrast may have assessments done with non-contrast computed tomography or MRI.
11 November 2015	Protocol was amended to clarify that a wash-out period of at least 4 weeks or five half-lives, whichever is longer, of any systemic immunomodulatory agent is required prior to enrollment.
15 June 2016	Protocol was amended to add a co-primary endpoint of overall survival (OS) to the progression-free survival (PFS) primary endpoint. For patients consented and randomized to Arm B after Ethics Committee or Institutional Review Board approval of Protocol GO29537, Version 5 at each respective site, the option for crossover to atezolizumab maintenance therapy has been removed to enable the comparative analyses of the two treatment arms. Patients randomized to Arm B who were consented under previous versions of this protocol prior to the approval of Version 5 will continue to have the option for crossover to atezolizumab maintenance therapy. The total number of patients to be randomized in the study has increased from 550 patients to 650 patients to ensure that the study is adequately powered for the comparative analyses. Erlotinib switch maintenance therapy has been removed from the protocol. A secondary efficacy objective and outcome measure has been added to evaluate the efficacy of atezolizumab + carboplatin + nab-paclitaxel compared with carboplatin + nab-paclitaxel as measured by investigator-assessed time to response (TTR) according to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) for both the intent-to-treat (ITT) and programmed death−ligand 1(PD-L1)−selected populations.

01 March 2017	Protocol was amended to include change to the primary analysis populations for the co-primary endpoints of progression-free survival (PFS) and overall survival (OS). OS will be analyzed in the intent-to-treat (ITT) population. PFS will be analyzed in the ITT population and a population with a defined level of expression of a PD-L1 and T-effector gene signature in tumor tissue as determined by an RNA-based assay. Patients with known sensitizing EGFR mutations or ALK translocations will be excluded from the primary analysis populations. The analyses of PFS and OS in all randomized patients will be conducted as secondary analyses. Additional censoring rule for the primary endpoint of PFS for U.S. registration purposes has been removed. The statistical testing procedures have been amended to reflect the change in analysis populations. All endpoints (secondary and exploratory) based on the review by an Independent Review Facility (IRF) have been removed.
24 October 2018	Protocol was amended to correct the end of study definition corrected. This correction ensures that the study continues until last patient, last visit or until the Sponsor terminates the study. The inclusion criterion that addresses female contraception has been modified to specify when women must refrain from donating eggs.
29 March 2019	Protocol was amended to clarify the inclusion criterion on contraception. In addition, reporting for serious adverse events and adverse events of special interest has been extended to 90 days after last dose of study treatment or until initiation of a new anticancer therapy, whichever occurs first.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported