Clinical trial results:
A Randomized, Double-Blind, Phase III Study of Pembrolizumab (MK-3475) plus Chemotherapy vs Placebo plus Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer

Summary

EudraCT number	2016-001432-35
Trial protocol	DE DK IE ES CZ HU BE NL PL FR
Global end of trial date	30 October 2023

Results information

Result version number	v1 (current)
This version publication date	14 November 2024
First version publication date	14 November 2024

Trial information

Trial identification

Sponsor protocol code	MK-3475-355

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02819518
WHO universal trial number (UTN)	-
Other trial identifiers	MSD: KEYNOTE-355

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC.
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC., ClinicalTrialsDisclosure@msd.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	30 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2021
Global end of trial reached?	Yes
Global end of trial date	30 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study will consist of two parts.
In Part 1, the safety of pembrolizumab (MK-3475) in combination with one of three different chemotherapies will be assessed in the treatment of locally recurrent inoperable or metastatic triple negative breast cancer (TNBC), which has not been previously treated with chemotherapy.

In Part 2, the safety and efficacy of pembrolizumab plus background chemotherapy will be assessed compared to the safety and efficacy of placebo plus background chemotherapy in the treatment of locally recurrent inoperable or metastatic TNBC, which has not been previously treated with chemotherapy.

The primary objective of Part 1 is to evaluate the safety and tolerability of the 3 pembrolizumab and chemotherapy combinations. The primary objectives of Part 2 are to compare the progression-free survival (PFS) and the overall survival (OS) of pembrolizumab and chemotherapy to placebo and chemotherapy.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	80 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 19
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Brazil: 57
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Chile: 27
Country: Number of subjects enrolled	Colombia: 21
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Denmark: 12

Country: Number of subjects enrolled	France: 29
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	Ireland: 10
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 91
Country: Number of subjects enrolled	Korea, Republic of: 32
Country: Number of subjects enrolled	Malaysia: 24
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Poland: 56
Country: Number of subjects enrolled	Russian Federation: 37
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Taiwan: 21
Country: Number of subjects enrolled	Türkiye: 41
Country: Number of subjects enrolled	Ukraine: 70
Country: Number of subjects enrolled	United Kingdom: 38
Country: Number of subjects enrolled	United States: 78
Worldwide total number of subjects	882
EEA total number of subjects	235

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)	688
From 65 to 84 years	193
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

35 participants were randomized to Part 1 (Safety Run-in) of the study, and 847 participants were randomized in Part 2 (phase 3) of the study. Twelve participants randomized to the Part 2: Pembrolizumab + Chemotherapy arm received a second course of pembrolizumab at the investigator's discretion.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Pembrolizumab + Nab-Paclitaxel

Arm description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	ABRAXANE®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle

Arm title	Part 1: Pembrolizumab + Paclitaxel

Arm description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	TAXOL®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle

Arm title	Part 1: Pembrolizumab + Gemcitabine/Carboplatin

Arm description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS gemcitabine/carboplatin (gemcitabine) and an Area Under the Curve (AUC) 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle

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

Dosage and administration details:

Area Under the Curve (AUC) 2 on Days 1 and 8 of each 21-day cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	GEMZAR®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine1000 mg/m^2 on Days 1 and 8 of each 21-day cycle.

Arm title	Part 2: Pembrolizumab + Chemotherapy

Arm description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle. Qualified participants who received first course of pembrolizumab but continued to experience disease progression were eligible to initiate a second course of pembrolizumab IV Q3W for up to 17 administrations (up to ~1 year).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle

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

Dosage and administration details:

one of three background chemotherapy regimens at investigator's discretion: 1) nabpaclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28- day cycle, OR 3)
gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.

Arm title	Part 2: Placebo + Chemotherapy

Arm description:

Participants received placebo (normal saline) IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle

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

Dosage and administration details:

one of three background chemotherapy regimens at investigator's discretion: 1) nabpaclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28- day cycle, OR 3)
gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.

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

Dosage and administration details:

Participants receive placebo (normal saline) IV on Day 1 of each 21-day cycle

Number of subjects in period 1	Part 1: Pembrolizumab + Nab-Paclitaxel	Part 1: Pembrolizumab + Paclitaxel	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Started	11	14	10
Completed	0	0	0
Not completed	11	14	10
Adverse event, serious fatal	9	12	9
Consent withdrawn by subject	-	-	-
Sponsor Decision	1	1	-
Transferred to extension study	1	1	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy
Started	566	281
Completed	0	0
Not completed	566	281
Adverse event, serious fatal	475	244
Consent withdrawn by subject	25	8
Sponsor Decision	34	17
Transferred to extension study	32	11
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Pembrolizumab + Nab-Paclitaxel
Reporting group description:	
Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.	
Reporting group title	Part 1: Pembrolizumab + Paclitaxel
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.	
Reporting group title	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS gemcitabine/carboplatin (gemcitabine) and an Area Under the Curve (AUC) 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.	
Reporting group title	Part 2: Pembrolizumab + Chemotherapy
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle. Qualified participants who received first course of pembrolizumab but continued to experience disease progression were eligible to initiate a second course of pembrolizumab IV Q3W for up to 17 administrations (up to ~1 year).	
Reporting group title	Part 2: Placebo + Chemotherapy
Reporting group description:	
Participants received placebo (normal saline) IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle	

Reporting group values	Part 1: Pembrolizumab + Nab-Paclitaxel	Part 1: Pembrolizumab + Paclitaxel	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Number of subjects	11	14	10
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)	7	8	6
From 65-84 years	4	6	4
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	54.6	60.4	59.6
standard deviation	± 13.5	± 15.3	± 11.7

Sex: Female, Male Units: Participants			
Female	11	14	10
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	7	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	6	7	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	9	14	10
Unknown or Not Reported	1	0	0
Programmed Cell Death Ligand 1 (PD-L1) Status (Combined Positive Score [CPS] Cutoff of 1)			
PD-L1 protein expression in triple-negative breast cancer (TNBC) is determined by using CPS, which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100. The number of participants with PD-L1 Status CPS<1 and CPS≥1 at baseline is presented.			
Units: Subjects			
PD-L1 CPS ≥1	8	12	7
PD-L1 CPS <1	3	2	3
PD-L1 Status (CPS Cutoff of 10)			
PD-L1 protein expression in TNBC is determined by using CPS, which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100. The number of participants with PD-L1 Status CPS<10 and CPS≥10 at baseline is presented.			
Units: Subjects			
PD-L1 CPS ≥10	1	9	4
PD-L1 CPS <10	10	5	6

Reporting group values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy	Total
Number of subjects	566	281	882
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)	443	224	688
From 65-84 years	122	57	193
85 years and over	1	0	1

Age Continuous Units: Years			
arithmetic mean	53.5	53.0	
standard deviation	± 12.7	± 12.7	-
Sex: Female, Male Units: Participants			
Female	566	281	882
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	11	1	12
Asian	123	52	190
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	20	17	38
White	384	195	598
More than one race	11	8	19
Unknown or Not Reported	17	8	25
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	116	48	165
Not Hispanic or Latino	423	218	674
Unknown or Not Reported	27	15	43
Programmed Cell Death Ligand 1 (PD-L1) Status (Combined Positive Score [CPS] Cutoff of 1)			
PD-L1 protein expression in triple-negative breast cancer (TNBC) is determined by using CPS, which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100. The number of participants with PD-L1 Status CPS<1 and CPS≥1 at baseline is presented.			
Units: Subjects			
PD-L1 CPS ≥1	425	211	663
PD-L1 CPS <1	141	70	219
PD-L1 Status (CPS Cutoff of 10)			
PD-L1 protein expression in TNBC is determined by using CPS, which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100. The number of participants with PD-L1 Status CPS<10 and CPS≥10 at baseline is presented.			
Units: Subjects			
PD-L1 CPS ≥10	220	103	337
PD-L1 CPS <10	346	178	545

End points

End points reporting groups

Reporting group title	Part 1: Pembrolizumab + Nab-Paclitaxel
Reporting group description:	
Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.	
Reporting group title	Part 1: Pembrolizumab + Paclitaxel
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.	
Reporting group title	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS gemcitabine/carboplatin (gemcitabine) and an Area Under the Curve (AUC) 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.	
Reporting group title	Part 2: Pembrolizumab + Chemotherapy
Reporting group description:	
Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle. Qualified participants who received first course of pembrolizumab but continued to experience disease progression were eligible to initiate a second course of pembrolizumab IV Q3W for up to 17 administrations (up to ~1 year).	
Reporting group title	Part 2: Placebo + Chemotherapy
Reporting group description:	
Participants received placebo (normal saline) IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle	
Subject analysis set title	As treated: Pembrolizumab + Nab-Paclitaxel
Subject analysis set type	Safety analysis
Subject analysis set description:	
One participant randomized did not receive treatment. 3 participants randomized to Pembrolizumab + Paclitaxel group received Pembrolizumab + Nab-Paclitaxel treatment in error	
Subject analysis set title	As Treated: Pembrolizumab + Paclitaxel
Subject analysis set type	Safety analysis
Subject analysis set description:	
3 participants randomized to Pembrolizumab + Paclitaxel received pembrolizumab + Nab-Paclitaxel in error; 1 participant received Pembrolizumab + Gemcitabine/Carboplatin in error	
Subject analysis set title	As treated: Pembrolizumab + Gemcitabine/Carboplatin
Subject analysis set type	Safety analysis
Subject analysis set description:	
1 participant randomized to Pembrolizumab + Paclitaxel group received Pembrolizumab + Gemcitabine/Carboplatin in error	
Subject analysis set title	As treated: Pembrolizumab + Chemotherapy
Subject analysis set type	Safety analysis
Subject analysis set description:	
4 participants were randomized but not treated	
Subject analysis set title	As Treated: Placebo + Chemotherapy
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants as treated	

Primary: Part 1: Percentage of Participants Who Experienced an Adverse Event (AE) - All Participants

End point title	Part 1: Percentage of Participants Who Experienced an Adverse Event (AE) - All Participants[1]

End point description:

An AE is defined as any unfavorable and unintended sign, symptom, disease, or worsening of preexisting condition temporally associated with study treatment and irrespective of causality to study treatment. The population analyzed included all randomly assigned participants who received at least 1 dose of study intervention were included in the group corresponding to the study intervention actually received. Four participants assigned to the pembrolizumab + paclitaxel group received incorrect chemotherapy in error: 3 participants received pembrolizumab + nab-paclitaxel and 1 received pembrolizumab + gemcitabine/carboplatin.

End point type	Primary

End point timeframe:

Up to approximately 39 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end point only included participants in Part 2 of the study.

End point values	As treated: Pembrolizumab + Nab-Paclitaxel	As Treated: Pembrolizumab + Paclitaxel	As treated: Pembrolizumab + Gemcitabine/Carboplatin	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	10	11	
Units: Percentage of Participants				
number (not applicable)	100.0	100.0	100.0	

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Percentage of Participants Who Discontinued Study Drug Due to an AE - All Participants

End point title	Part 1: Percentage of Participants Who Discontinued Study Drug Due to an AE - All Participants[2]

End point description:

An AE is defined as any unfavorable and unintended sign, symptom, disease, or worsening of preexisting condition temporally associated with study treatment and irrespective of causality to study treatment. The population analyzed included all randomly assigned participants who received at least 1 dose of study intervention were included in the group corresponding to the study intervention actually received. Four participants assigned to the pembrolizumab + paclitaxel group received incorrect chemotherapy in error: 3 participants received pembrolizumab + nab-paclitaxel and 1 received pembrolizumab + gemcitabine/carboplatin.

End point type	Primary

End point timeframe:

Up to approximately 39 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, the end point only included participants in Part 2 of the study.

End point values	As treated: Pembrolizumab + Nab-Paclitaxel	As Treated: Pembrolizumab + Paclitaxel	As treated: Pembrolizumab + Gemcitabine/Carboplatin	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	10	11	
Units: Percentage of Participants				
number (not applicable)	38.5	50.0	27.3	

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Progression-Free Survival (PFS) - All Participants

End point title	Part 2: Progression-Free Survival (PFS) - All Participants[3]

End point description:

Progression-free survival was defined as the time from randomization to the first documented progressive disease (PD) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) based on assessments by blinded independent central review (BICR) or death due to any cause, whichever occurs first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of ≥5 mm. The appearance of one or more new lesions was also considered PD. Participants were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment

End point type	Primary

End point timeframe:

Up to approximately 53 months

Notes:

[3] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	566	281		
Units: Months				
median (confidence interval 95%)	7.5 (6.3 to 7.7)	5.6 (5.4 to 7.2)		

Statistical analyses

Statistical analysis title	Hazard Ratio of PFS

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by chemotherapy on study, tumor PD-L1 status, and prior treatment with same class of chemotherapy in the (neo)adjuvant setting.

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	847
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.98

Notes:

[4] - One-sided p-value based on log-rank test stratified by chemotherapy (taxane versus [vs] gemcitabine/carboplatin), tumor PD-L1 status (CPS ≥1 vs CPS <1) and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs. no).

Primary: Part 2: PFS - Participants with PD-L1 CPS ≥10 Tumors

End point title	Part 2: PFS - Participants with PD-L1 CPS ≥10 Tumors

End point description:

Progression-free survival was defined as the time from randomization to the first documented PD per RECIST 1.1 based on assessments by BICR or death due to any cause, whichever occurs first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of ≥5 mm. The appearance of one or more new lesions was also considered PD.
Participants with PD-L1 CPS ≥10 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment,

End point type	Primary

End point timeframe:

Up to approximately 53 months

End point values	As treated: Pembrolizumab + Chemotherapy	As Treated: Placebo + Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	103		
Units: Months				
median (confidence interval 95%)	9.7 (7.6 to 11.3)	5.6 (5.3 to 7.5)		

Statistical analyses

Statistical analysis title	Hazard Ratio of PFS

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by chemotherapy on study, and prior treatment with same class of chemotherapy in the (neo)adjuvant setting.

Comparison groups	As Treated: Placebo + Chemotherapy v As treated: Pembrolizumab + Chemotherapy

Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0018 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.88

Notes:

[5] - One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Primary: Part 2: PFS - Participants with Programmed Cell Death-Ligand 1 (PD-L1) Combined Positive Score (CPS) ≥1 Tumors

End point title	Part 2: PFS - Participants with Programmed Cell Death-Ligand 1 (PD-L1) Combined Positive Score (CPS) ≥1 Tumors[6]

End point description:

Progression-free survival was defined as the time from randomization to the first documented PD per RECIST 1.1 based on assessments by BICR or death due to any cause, whichever occurs first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of ≥5 mm. The appearance of one or more new lesions was also considered PD.
Participants with PD-L1 CPS ≥1 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment.

End point type	Primary

End point timeframe:

Up to approximately 53 months

Notes:

[6] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	211		
Units: Months				
median (confidence interval 95%)	7.6 (6.6 to 8.0)	5.6 (5.4 to 7.4)		

Statistical analyses

Statistical analysis title	Hazard Ratio of PFS

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by chemotherapy on study, and prior treatment with same class of chemotherapy in the (neo)adjuvant setting.

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0016 [7]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.91

Notes:

[7] - One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Primary: Part 2: Overall Survival (OS) - All Participants

End point title	Part 2: Overall Survival (OS) - All Participants[8]

End point description:

Overall survival is defined as the time from randomization to death due to any cause. Participants without documented death at the time of the analysis were censored at the date of the last follow-up. Participants were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment.

End point type	Primary

End point timeframe:

Up to approximately 53 months

Notes:

[8] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	566	281		
Units: Months				
median (confidence interval 95%)	17.2 (15.3 to 19.0)	15.5 (13.9 to 17.2)		

Statistical analyses

Statistical analysis title	Hazard Ratio of OS

Statistical analysis description:

One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), tumor PD-L1 status (CPS ≥1 vs CPS <1) and prior treatment with same class of chemotherapy
in the (neo)adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	847
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0797 [9]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.05

Notes:

[9] - One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), tumor PD-L1 status (CPS ≥1 vs CPS <1) and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Primary: Part 2: OS - Participants with PD-L1 CPS ≥1 Tumors

End point title	Part 2: OS - Participants with PD-L1 CPS ≥1 Tumors[10]

End point description:

Overall survival is defined as the time from randomization to death due to any cause. Participants without documented death at the time of the analysis were censored at the date of the last follow-up. Participants with PD-L1 CPS ≥1 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment

End point type	Primary

End point timeframe:

Up to approximately 53 months

Notes:

[10] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	211		
Units: Months				
median (confidence interval 95%)	17.6 (15.5 to 19.5)	16.0 (12.8 to 17.4)		

Statistical analyses

Statistical analysis title	Hazard Ratio of OS

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by chemotherapy on study, and prior treatment with same class of chemotherapy in the (neo)adjuvant setting.

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0563 [11]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.04

Notes:

[11] - One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Primary: Part 2: OS - Participants with PD-L1 CPS ≥10 Tumors

End point title	Part 2: OS - Participants with PD-L1 CPS ≥10 Tumors[12]

End point description:

Overall survival is defined as the time from randomization to death due to any cause. Participants without documented death at the time of the analysis were censored at the date of the last follow-up. Participants with PD-L1 CPS ≥10 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment.

End point type	Primary

End point timeframe:

Up to approximately 53 months

Notes:

[12] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	103		
Units: Months				
median (confidence interval 95%)	23.0 (19.0 to 26.3)	16.1 (12.6 to 18.8)		

Statistical analyses

Statistical analysis title	Hazard Ratio of OS

Statistical analysis description:

Based on Cox regression model with treatment as a covariate stratified by chemotherapy on study, and prior treatment with same class of chemotherapy in the (neo)adjuvant setting.

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0093 [13]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.95

Notes:

[13] - One-sided p-value based on log-rank test stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Secondary: Part 2: Objective Response Rate (ORR) - All Participants

End point title	Part 2: Objective Response Rate (ORR) - All Participants[14]

End point description:

Objective response rate is defined as the percentage of participants in the analysis population who have a complete response (CR: disappearance of all target lesions) or partial response (PR: at least a 30% decrease in the sum of diameters of target lesions). The percentage of participants who experienced a CR or PR as assessed by BICR based on RECIST 1.1 is presented.
Participants were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

Notes:

[14] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	566	281		
Units: Percentage of Participants				
number (confidence interval 95%)	40.8 (36.7 to 45.0)	37.0 (31.4 to 42.9)		

Statistical analyses

Statistical analysis title	Difference in ORR (%) vs. Control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), tumor PD-L1 status (CPS ≥1 vs CPS <1) and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	847
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1413
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR (%) vs. Control
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	10.6

Secondary: Part 2: ORR - Participants With PD-L1 CPS ≥1 Tumors

End point title	Part 2: ORR - Participants With PD-L1 CPS ≥1 Tumors[15]

End point description:

Objective response rate is defined as the percentage of participants in the analysis population who have a complete response (CR: disappearance of all target lesions) or partial response (PR: at least a 30% decrease in the sum of diameters of target lesions). The percentage of participants who experienced a CR or PR as assessed by BICR based on RECIST 1.1 is presented.
Participants with PD-L1 CPS ≥1 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment

End point type	Secondary

End point timeframe:

Up to approximately 53 months

Notes:

[15] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	211		
Units: Percentage of Participants				
number (confidence interval 95%)	44.9 (40.1 to 49.8)	38.9 (32.2 to 45.8)		

Statistical analyses

Statistical analysis title	Difference in ORR (%) vs. Control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0725
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR (%) vs. Control
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	14

Secondary: Part 2: ORR - Participants With PD-L1 CPS ≥10 Tumors

End point title	Part 2: ORR - Participants With PD-L1 CPS ≥10 Tumors[16]

End point description:

Objective response rate is defined as the percentage of participants in the analysis population who have a complete response (CR: disappearance of all target lesions) or partial response (PR: at least a 30% decrease in the sum of diameters of target lesions). The percentage of participants who experienced a CR or PR as assessed by BICR based on RECIST 1.1 is presented.
Participants with PD-L1 CPS ≥10 tumors were analyzed in the treatment arm to which they were randomly assigned, regardless of whether they received treatment.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

Notes:

[16] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	103		
Units: Percentage of Participants				
number (confidence interval 95%)	52.7 (45.9 to 59.5)	40.8 (31.2 to 50.9)		

Statistical analyses

Statistical analysis title	Difference in ORR(%) vs. Control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin) and prior treatment with same class of chemotherapy in the (neo)adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0213
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR(%) vs. Control
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	23.4

Secondary: Part 2: DOR – Participants With PD-L1 CPS ≥1 Tumors

End point title	Part 2: DOR – Participants With PD-L1 CPS ≥1 Tumors[17]

End point description:

For participants who demonstrate a confirmed CR (Disappearance of all target lesions) or confirmed PR (At least a 30% decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR is defined as the time from first documented evidence of CR or PR until progressive disease (PD) or death due to any cause, whichever occurs first. PD was defined as at least a 20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered PD. A value of 9999 indicates median, upper limit, lower limit not reached due to insufficient number of responding participants with relapse. The population analyzed included all randomized participants, regardless of whether they received study treatment, who demonstrated a confirmed response (CR or PR). Participants were included in the treatment arm to which they were randomized.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

Notes:

[17] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	82		
Units: Months				
median (full range (min-max))	9999 (9999 to 9999)	6.8 (1.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Duration of Response (DOR) - All Participants

End point title	Part 2: Duration of Response (DOR) - All Participants[18]

End point description:

For participants who demonstrate a confirmed CR (Disappearance of all target lesions) or confirmed PR (At least a 30% decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR is defined as the time from first documented evidence of CR or PR until progressive disease (PD) or death due to any cause, whichever occurs first. PD was defined as at least a 20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered PD. A value of 9999 indicates median, upper limit, lower limit not reached due to insufficient number of responding participants with relapse. The population analyzed included all randomized participants, regardless of whether they received study treatment, who demonstrated a confirmed response (CR or PR). Participants were included in the treatment arm to which they were randomized.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	104		
Units: Months				
median (full range (min-max))	9999 (9999 to 9999)	6.5 (1.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: DOR – Participants With PD-L1 CPS ≥10 Tumors

End point title	Part 2: DOR – Participants With PD-L1 CPS ≥10 Tumors[19]

End point description:

For participants who demonstrate a confirmed CR (Disappearance of all target lesions) or confirmed PR (At least a 30% decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR is defined as the time from first documented evidence of CR or PR until progressive disease (PD) or death due to any cause, whichever occurs first. PD was defined as at least a 20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered PD. A value of 9999 indicates median, upper limit, lower limit not reached due to insufficient number of responding participants with relapse. The population analyzed included all randomized participants, regardless of whether they received study treatment, who demonstrated a confirmed response (CR or PR). Participants were included in the treatment arm to which they were randomized.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	42		
Units: Months				
median (full range (min-max))	9999 (9999 to 9999)	7.3 (1.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Disease Control Rate (DCR) - All Participants

End point title	Part 2: Disease Control Rate (DCR) - All Participants[20]

End point description:

Disease control rate is defined as the percentage of participants who have achieved CR (disappearance of all target lesions) or PR (At least a 30% decrease in the sum of diameters of target lesions) or have demonstrated stable disease (SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease [PD: At least a 20% increase in the sum of diameters of target lesions and an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered PD]) for at least 24 weeks, based on assessments by BICR per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to approximately 53 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	566	281		
Units: Percentage of Participants				
number (confidence interval 95%)	56.0 (51.8 to 60.1)	51.2 (45.2 to 57.2)		

Statistical analyses

Statistical analysis title	Difference in DCR (%) vs. control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin), tumor PD-L1 status (CPS ≥1 vs CPS <1) and prior treatment with same class of chemotherapy in the (neo) adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	847
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0966
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in DCR (%) vs. control
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	11.8

Secondary: Part 2: DCR – Participants With PD-L1 CPS ≥1 Tumors

End point title	Part 2: DCR – Participants With PD-L1 CPS ≥1 Tumors[21]

End point description:

Disease control rate is defined as the percentage of participants who have achieved CR (disappearance of all target lesions) or PR (At least a 30% decrease in the sum of diameters of target lesions) or have demonstrated stable disease (SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease [PD: At least a 20% increase in the sum of diameters of target lesions and an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered PD]) for at least 24 weeks, based on assessments by BICR per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to approximately 53 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	211		
Units: Percentage of Participants				
number (confidence interval 95%)	58.6 (53.7 to 63.3)	53.6 (46.6 to 60.4)		

Statistical analyses

Statistical analysis title	Difference in DCR (%) vs. Control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin) and prior treatment with same class of chemotherapy in the (neo) adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	636
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1164
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in DCR (%) vs. Control
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	13.1

Secondary: Part 2: DCR – Participants With PD-L1 CPS ≥10 Tumors

End point title	Part 2: DCR – Participants With PD-L1 CPS ≥10 Tumors[22]

End point description:

Disease control rate is defined as the percentage of participants who have achieved CR (disappearance of all target lesions) or PR (At least a 30% decrease in the sum of diameters of target lesions) or have demonstrated stable disease (SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease [PD: At least a 20% increase in the sum of diameters of target lesions and an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered PD]) for at least 24 weeks, based on assessments by BICR per RECIST 1.1.

End point type	Secondary

End point timeframe:

Up to approximately 53 months

Notes:

[22] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	103		
Units: Percentage of Participants				
number (confidence interval 95%)	65.0 (58.3 to 71.3)	54.4 (44.3 to 64.2)		

Statistical analyses

Statistical analysis title	Difference in DCR (%) vs. Control

Statistical analysis description:

Based on Miettinen & Nurminen method stratified by chemotherapy on study (taxane vs gemcitabine/carboplatin) and prior treatment with same class of chemotherapy in the (neo) adjuvant setting (yes vs no).

Comparison groups	Part 2: Pembrolizumab + Chemotherapy v Part 2: Placebo + Chemotherapy

Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0327
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in DCR (%) vs. Control
Point estimate	10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	22.3

Secondary: Part 2: Percentage of Participants Who Discontinued Study Drug Due to an AE- All Participants

End point title	Part 2: Percentage of Participants Who Discontinued Study Drug Due to an AE- All Participants[23]

End point description:

An AE is defined as any unfavorable and unintended sign, symptom, disease, or worsening of preexisting condition temporally associated with study treatment and irrespective of causality to study treatment.

End point type	Secondary

End point timeframe:

Up to approximately 81 months

Notes:

[23] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	281		
Units: Percentage of Participants				
number (not applicable)	20.5	13.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants Who Experienced an AE- All Participants

End point title	Part 2: Percentage of Participants Who Experienced an AE- All Participants[24]

End point description:

An AE is defined as any unfavorable and unintended sign, symptom, disease, or worsening of preexisting condition temporally associated with study treatment and irrespective of causality to study

treatment.

End point type	Secondary

End point timeframe:

Up to approximately 81 months

Notes:

[24] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	562	281		
Units: Percentage of Participants				
number (not applicable)	98.6	98.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score- All Participants

End point title	Part 2: Change from Baseline to Week 15 in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score- All Participants[25]

End point description:

The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant responses to the questions "How would you rate your overall health during the past week?" (Item 29) and “How would you rate your overall quality of life during the past week?” (Item 30) were scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores were standardized, so that scores range from 0 to 100. A higher score indicates a better overall health status. The change from baseline in EORTC QLQ-C30 Items 29 and 30 combined score are presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[25] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	554	278		
Units: Scores on a scale				

least squares mean (confidence interval 95%)	-3.52 (-5.61 to -1.42)	-2.15 (-4.97 to 0.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in EORTC QLQ-C30 Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score - Participants With PD-L1 CPS ≥1 Tumors

End point title	Part 2: Change from Baseline to Week 15 in EORTC QLQ-C30 Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score - Participants With PD-L1 CPS ≥1 Tumors[26]

End point description:

The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant responses to the questions "How would you rate your overall health during the past week?" (Item 29) and "How would you rate your overall quality of life during the past week?" (Item 30) were scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores were standardized, so that scores range from 0 to 100. A higher score indicates a better overall health status. The change from baseline in EORTC QLQ-C30 Items 29 and 30 combined score are presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[26] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	415	208		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-3.92 (-6.42 to -1.44)	-3.15 (-6.54 to 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in EORTC QLQ-C30 Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score-Participants With PD-L1 CPS ≥10 Tumors

End point title	Part 2: Change from Baseline to Week 15 in EORTC QLQ-C30 Global Health Status (Item 29) and Quality of Life (Item 30) Combined Score-Participants With PD-L1 CPS ≥10 Tumors[27]

End point description:

The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant

responses to the questions "How would you rate your overall health during the past week?" (Item 29) and “How would you rate your overall quality of life during the past week?” (Item 30) were scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores were standardized, so that scores range from 0 to 100. A higher score indicates a better overall health status. The change from baseline in EORTC QLQ-C30 Items 29 and 30 combined score are presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[27] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	100		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-2.69 (-5.86 to 0.48)	-0.88 (-5.41 to 3.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in Systemic Therapy Side Effects Using the EORTC Breast Cancer-Specific Quality of Life Questionnaire (QLQ-BR23)-All Participants

End point title	Part 2: Change from Baseline to Week 15 in Systemic Therapy Side Effects Using the EORTC Breast Cancer-Specific Quality of Life Questionnaire (QLQ-BR23)-All Participants[28]

End point description:

EORTC-QLQ-BR23 is a 23-item breast cancer-specific companion module to the EORTC-QLQ-C30 and consists of four functional scales (body image, sexual enjoyment, sexual functioning, future perspective) and four symptom scales (systemic therapy side effects, upset by hair loss, arm symptoms, breast symptoms). Participant responses to 7 questions about their systemic therapy side effects were scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A higher score denotes worse symptoms for the systemic therapy side effects symptom scale. The change from baseline in systemic therapy side effects (EORTC QLQ-BR23 Items 1-4, 6, 7, and 8) score is presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[28] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	554	278		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	12.50 (10.84 to 14.15)	12.36 (10.06 to 14.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in Systemic Therapy Side Effects Using the EORTC QLQ-BR23 - Participants with PD-L1 CPS ≥1 Tumors

End point title	Part 2: Change from Baseline to Week 15 in Systemic Therapy Side Effects Using the EORTC QLQ-BR23 - Participants with PD-L1 CPS ≥1 Tumors[29]

End point description:

EORTC-QLQ-BR23 is a 23-item breast cancer-specific companion module to the EORTC-QLQ-C30 and consists of four functional scales (body image, sexual enjoyment, sexual functioning, future perspective) and four symptom scales (systemic therapy side effects, upset by hair loss, arm symptoms, breast symptoms). Participant responses to 7 questions about their systemic therapy side effects were scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A higher score denotes worse symptoms for the systemic therapy side effects symptom scale. The change from baseline in systemic therapy side effects (EORTC QLQ-BR23 Items 1-4, 6, 7, and 8) score is presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[29] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	415	208		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	13.00 (11.08 to 14.91)	11.86 (9.17 to 14.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline to Week 15 in Systemic Therapy Side

Effects Using the EORTC QLQ-BR23- Participants with PD-L1 CPS ≥10 Tumors

End point title	Part 2: Change from Baseline to Week 15 in Systemic Therapy Side Effects Using the EORTC QLQ-BR23- Participants with PD-L1 CPS ≥10 Tumors[30]

End point description:

EORTC-QLQ-BR23 is a 23-item breast cancer-specific companion module to the EORTC-QLQ-C30 and consists of four functional scales (body image, sexual enjoyment, sexual functioning, future perspective) and four symptom scales (systemic therapy side effects, upset by hair loss, arm symptoms, breast symptoms). Participant responses to 7 questions about their systemic therapy side effects are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. A higher score denotes worse symptoms for the systemic therapy side effects symptom scale. The change from baseline in systemic therapy side effects (EORTC QLQ-BR23 Items 1-4, 6, 7, and 8) score is presented.

End point type	Secondary

End point timeframe:

Baseline and Week 15

Notes:

[30] - 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: Per protocol, the end point only included participants in Part 2 of the study.

End point values	Part 2: Pembrolizumab + Chemotherapy	Part 2: Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	100		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	13.56 (10.88 to 16.23)	13.26 (9.28 to 17.25)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 81 months

Adverse event reporting additional description:

All participants who received > or =1 dose of study intervention corresponding to the intervention received. 4 participants assigned to the pembrolizumab + paclitaxel group received incorrect chemotherapy in error. Per protocol, “Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Part 1: Pembrolizumab + Nab-Paclitaxel

Reporting group description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle PLUS nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.

Reporting group title	Part 1: Pembrolizumab + Paclitaxel

Reporting group description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle.

Reporting group title	Part 2: Placebo + Chemotherapy

Reporting group description:

Participants received placebo (normal saline) IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel 100 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel 90 mg/m^2 IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin 1000 mg/m^2 (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle

Reporting group title	Part 2: Pembrolizumab + Chemotherapy (First Course)

Reporting group description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS one of three background chemotherapy regimens at investigator's discretion: 1) nab-paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, 2) paclitaxel IV on Days 1, 8 and 15 of each 28-day cycle, OR 3) gemcitabine/carboplatin (gemcitabine) and an AUC 2 (carboplatin) on Days 1 and 8 of each 21-day cycle. Qualified participants who received first course of pembrolizumab but continued to experience disease progression were eligible to initiate a second course of pembrolizumab IV Q3W for up to 17 administrations (up to ~1 year).

Reporting group title	Part 2: Pembrolizumab + Chemotherapy (Second Course)

Reporting group description:

Eligible participants received up to 17 additional administrations (up to approximately 1year) of pembrolizumab 200 mg IV on day 1 of each 21-day cycle.

Reporting group title	Part 1: Pembrolizumab + Gemcitabine/Carboplatin

Reporting group description:

Participants received pembrolizumab 200 mg IV on Day 1 of each 21-day cycle PLUS gemcitabine/carboplatin (gemcitabine) and an Area Under the Curve (AUC) 2 (carboplatin) on Days 1 and 8 of each 21-day cycle.

Serious adverse events	Part 1: Pembrolizumab + Nab-Paclitaxel	Part 1: Pembrolizumab + Paclitaxel	Part 2: Placebo + Chemotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)	4 / 10 (40.00%)	68 / 281 (24.20%)
number of deaths (all causes)	11	9	249
number of deaths resulting from adverse events	0	1	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Assisted suicide			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Drug withdrawal syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fat necrosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal uterine bleeding			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchostenosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood corticotrophin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cortisol decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion-related acute lung injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardio-respiratory arrest			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar haemorrhage			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Cheilitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steatohepatitis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney enlargement			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scleroderma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	7 / 281 (2.49%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Viral infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			

subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Pembrolizumab + Chemotherapy (First Course)	Part 2: Pembrolizumab + Chemotherapy (Second Course)	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Total subjects affected by serious adverse events			
subjects affected / exposed	169 / 562 (30.07%)	3 / 12 (25.00%)	9 / 11 (81.82%)
number of deaths (all causes)	480	5	9
number of deaths resulting from adverse events	17	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Surgical and medical procedures			
Assisted suicide			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Drug withdrawal syndrome			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fat necrosis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Face oedema			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	7 / 562 (1.25%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	7 / 8	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abnormal uterine bleeding			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchostenosis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	8 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood corticotrophin increased			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cortisol decreased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Liver function test abnormal			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic enzymes increased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Limb injury			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion-related acute lung injury			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar haemorrhage			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous sinus thrombosis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelopathy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	6 / 7	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences causally related to treatment / all	12 / 12	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	7 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	12 / 14	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Papilloedema			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Cheilitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	10 / 562 (1.78%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	10 / 12	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steatohepatitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Kidney enlargement			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	4 / 562 (0.71%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scleroderma			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Polyarthritis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cellulitis			

subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 11	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	1 / 562 (0.18%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			

subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part 1: Pembrolizumab + Nab-Paclitaxel	Part 1: Pembrolizumab + Paclitaxel	Part 2: Placebo + Chemotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	10 / 10 (100.00%)	273 / 281 (97.15%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	1	0	2
Flushing			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences (all)	0	1	3
Deep vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	9 / 281 (3.20%)
occurrences (all)	3	0	10
Hot flush			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	10 / 281 (3.56%)
occurrences (all)	1	2	14
Lymphoedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	11 / 281 (3.91%)
occurrences (all)	0	0	11
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Infusion site pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Infusion site extravasation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Fatigue			

subjects affected / exposed	1 / 13 (7.69%)	2 / 10 (20.00%)	96 / 281 (34.16%)
occurrences (all)	1	3	119
Chills			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	7 / 281 (2.49%)
occurrences (all)	1	1	7
Chest pain			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	17 / 281 (6.05%)
occurrences (all)	2	1	20
Asthenia			
subjects affected / exposed	6 / 13 (46.15%)	3 / 10 (30.00%)	47 / 281 (16.73%)
occurrences (all)	16	8	84
Thirst			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	0	1	2
Oedema peripheral			
subjects affected / exposed	5 / 13 (38.46%)	0 / 10 (0.00%)	29 / 281 (10.32%)
occurrences (all)	5	0	42
Oedema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	14 / 281 (4.98%)
occurrences (all)	1	0	21
Mucosal dryness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	14 / 281 (4.98%)
occurrences (all)	0	1	25
Pyrexia			
subjects affected / exposed	3 / 13 (23.08%)	2 / 10 (20.00%)	55 / 281 (19.57%)
occurrences (all)	3	2	85
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0

Drug hypersensitivity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	0 / 13 (0.00%)	2 / 10 (20.00%)	8 / 281 (2.85%)
occurrences (all)	0	3	16
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	14 / 281 (4.98%)
occurrences (all)	1	0	14
Female genital tract fistula			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Bronchostenosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	2 / 13 (15.38%)	4 / 10 (40.00%)	49 / 281 (17.44%)
occurrences (all)	2	4	60
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 10 (20.00%)	17 / 281 (6.05%)
occurrences (all)	0	3	20
Haemoptysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 281 (0.71%)
occurrences (all)	0	1	2
Hydrothorax			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Nasal pruritus			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	18 / 281 (6.41%)
occurrences (all)	0	0	25
Pneumothorax			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	3
Productive cough			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	13 / 281 (4.63%)
occurrences (all)	1	1	15
Pulmonary embolism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	2	0	4
Sinus congestion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	0	0	4
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	2 / 10 (20.00%)	37 / 281 (13.17%)
occurrences (all)	1	3	44
Dyspnoea exertional			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	5 / 281 (1.78%)
occurrences (all)	0	1	6
Throat irritation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	0	0	4
Anxiety			
subjects affected / exposed	0 / 13 (0.00%)	2 / 10 (20.00%)	11 / 281 (3.91%)
occurrences (all)	0	2	11

Stress			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Persistent depressive disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 10 (20.00%)	28 / 281 (9.96%)
occurrences (all)	2	2	32
Depression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	13 / 281 (4.63%)
occurrences (all)	1	0	13
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	55 / 281 (19.57%)
occurrences (all)	1	2	84
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	46 / 281 (16.37%)
occurrences (all)	1	2	69
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	22 / 281 (7.83%)
occurrences (all)	1	0	28
Blood cholesterol increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Blood corticotrophin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	16 / 281 (5.69%)
occurrences (all)	0	0	17
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	1	0	3
Cortisol decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	8 / 281 (2.85%)
occurrences (all)	1	0	11
Haemoglobin decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	4
Lipase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 10 (30.00%)	11 / 281 (3.91%)
occurrences (all)	0	7	32
Weight increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	7 / 281 (2.49%)
occurrences (all)	0	1	8
White blood cell count decreased			
subjects affected / exposed	0 / 13 (0.00%)	5 / 10 (50.00%)	55 / 281 (19.57%)
occurrences (all)	0	20	211
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	4 / 10 (40.00%)	12 / 281 (4.27%)
occurrences (all)	2	5	13
Lymphocyte percentage decreased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 13 (15.38%)	5 / 10 (50.00%)	76 / 281 (27.05%)
occurrences (all)	2	17	310
Neutrophil percentage decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	0	1	9
Platelet count decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	44 / 281 (15.66%)
occurrences (all)	0	0	125
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Incision site pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	3
Wound complication			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Thermal burn			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 13 (15.38%)	5 / 10 (50.00%)	66 / 281 (23.49%)
occurrences (all)	3	7	104
Dysgeusia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	15 / 281 (5.34%)
occurrences (all)	1	0	18
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	3 / 10 (30.00%)	24 / 281 (8.54%)
occurrences (all)	1	4	33
Dementia Alzheimer's type			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	2	0	5
Mental impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	5 / 281 (1.78%)
occurrences (all)	1	0	5
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	6 / 281 (2.14%)
occurrences (all)	0	1	8
Presyncope			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	1	0	5
Polyneuropathy			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 13 (7.69%)	3 / 10 (30.00%)	20 / 281 (7.12%)
occurrences (all)	1	4	22
Peripheral motor neuropathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	0	0	2
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	15 / 281 (5.34%)
occurrences (all)	1	0	15
Neurotoxicity			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	4 / 281 (1.42%)
occurrences (all)	3	2	7
Neuropathy peripheral			
subjects affected / exposed	4 / 13 (30.77%)	2 / 10 (20.00%)	35 / 281 (12.46%)
occurrences (all)	6	2	50
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 13 (38.46%)	5 / 10 (50.00%)	140 / 281 (49.82%)
occurrences (all)	5	15	258
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	56 / 281 (19.93%)
occurrences (all)	0	0	155
Neutropenia			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	109 / 281 (38.79%)
occurrences (all)	3	21	384
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	0	0	15
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	50 / 281 (17.79%)
occurrences (all)	0	0	158
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	12 / 281 (4.27%)
occurrences (all)	1	1	13
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	5 / 281 (1.78%)
occurrences (all)	0	1	5
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	8 / 281 (2.85%)
occurrences (all)	1	0	8
Eye pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Eyelid cyst			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	8 / 281 (2.85%)
occurrences (all)	0	0	8
Eye pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences (all)	0	0	6
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	6 / 281 (2.14%)
occurrences (all)	0	1	6
Diarrhoea			
subjects affected / exposed	5 / 13 (38.46%)	2 / 10 (20.00%)	66 / 281 (23.49%)
occurrences (all)	9	3	134
Dental caries			

subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 281 (0.71%)
occurrences (all)	0	1	2
Constipation			
subjects affected / exposed	3 / 13 (23.08%)	3 / 10 (30.00%)	77 / 281 (27.40%)
occurrences (all)	3	3	97
Colitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences (all)	0	1	3
Anal fissure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 281 (0.71%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	16 / 281 (5.69%)
occurrences (all)	1	1	19
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	25 / 281 (8.90%)
occurrences (all)	0	1	28
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences (all)	0	0	7
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	10 / 281 (3.56%)
occurrences (all)	1	1	14
Gastritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	7 / 281 (2.49%)
occurrences (all)	0	1	7
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	16 / 281 (5.69%)
occurrences (all)	1	0	19
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	11 / 281 (3.91%)
occurrences (all)	0	0	12
Gingival bleeding			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 13 (23.08%)	2 / 10 (20.00%)	62 / 281 (22.06%)
occurrences (all)	5	2	107
Stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 10 (20.00%)	19 / 281 (6.76%)
occurrences (all)	0	2	22
Nausea			
subjects affected / exposed	6 / 13 (46.15%)	2 / 10 (20.00%)	130 / 281 (46.26%)
occurrences (all)	7	3	254
Large intestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	1	0	3
Hepatic function abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Butterfly rash			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	2	0	0
Alopecia			
subjects affected / exposed	4 / 13 (30.77%)	5 / 10 (50.00%)	97 / 281 (34.52%)
occurrences (all)	4	5	97
Dermatitis acneiform			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences (all)	0	0	7
Dermatitis contact			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	0	0	4
Nail discolouration			

subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	10 / 281 (3.56%)
occurrences (all)	1	1	10
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	10 / 281 (3.56%)
occurrences (all)	0	1	10
Dyshidrotic eczema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	11 / 281 (3.91%)
occurrences (all)	1	1	18
Erythema nodosum			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	4 / 281 (1.42%)
occurrences (all)	0	1	4
Drug eruption			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 281 (0.71%)
occurrences (all)	0	1	2
Onychalgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	1	0	4
Nail dystrophy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	1	1	1
Pigmentation disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0

Skin lesion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	1	0	4
Skin hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	0	1	1
Rash pruritic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	0	0	2
Rash papular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 13 (0.00%)	3 / 10 (30.00%)	10 / 281 (3.56%)
occurrences (all)	0	3	10
Pruritus			
subjects affected / exposed	3 / 13 (23.08%)	3 / 10 (30.00%)	32 / 281 (11.39%)
occurrences (all)	3	6	39
Rash			
subjects affected / exposed	2 / 13 (15.38%)	2 / 10 (20.00%)	34 / 281 (12.10%)
occurrences (all)	2	4	44
Urticaria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences (all)	0	2	4
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	4
Dysuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	1	0	3
Polyuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			

Hyperthyroidism			
subjects affected / exposed	1 / 13 (7.69%)	2 / 10 (20.00%)	4 / 281 (1.42%)
occurrences (all)	1	3	4
Adrenal insufficiency			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Hypophysitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Hypothyroidism			
subjects affected / exposed	1 / 13 (7.69%)	3 / 10 (30.00%)	9 / 281 (3.20%)
occurrences (all)	1	3	10
Thyroiditis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	0	1	1
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Coccydynia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	17 / 281 (6.05%)
occurrences (all)	0	1	21
Back pain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	41 / 281 (14.59%)
occurrences (all)	2	0	48
Arthritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences (all)	0	1	3
Arthralgia			

subjects affected / exposed	4 / 13 (30.77%)	1 / 10 (10.00%)	48 / 281 (17.08%)
occurrences (all)	4	1	73
Musculoskeletal chest pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	13 / 281 (4.63%)
occurrences (all)	1	1	16
Spinal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	0	0	2
Pain in jaw			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	2 / 281 (0.71%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	41 / 281 (14.59%)
occurrences (all)	3	0	47
Osteoporosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	20 / 281 (7.12%)
occurrences (all)	0	1	23
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 10 (30.00%)	34 / 281 (12.10%)
occurrences (all)	0	3	57
Musculoskeletal stiffness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	1 / 281 (0.36%)
occurrences (all)	0	1	1
Synovial cyst			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	5 / 281 (1.78%)
occurrences (all)	1	0	6
Gastrointestinal infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0

Hordeolum			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	1	0	2
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	8 / 281 (2.85%)
occurrences (all)	0	1	10
Lip infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	21 / 281 (7.47%)
occurrences (all)	3	0	28
Appendicitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	1	0	5
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	3 / 281 (1.07%)
occurrences (all)	0	1	13
Conjunctivitis viral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	3 / 281 (1.07%)
occurrences (all)	0	0	5
Erythema infectiosum			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	4 / 281 (1.42%)
occurrences (all)	0	1	6

Oropharyngeal candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Vulvovaginitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	2 / 281 (0.71%)
occurrences (all)	1	0	2
Viral infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	1	0	6
Viral diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 281 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	13 / 281 (4.63%)
occurrences (all)	2	1	14
Upper respiratory tract infection			
subjects affected / exposed	5 / 13 (38.46%)	3 / 10 (30.00%)	26 / 281 (9.25%)
occurrences (all)	5	4	36
Tonsillitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	1	0	4
Pharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	5 / 281 (1.78%)
occurrences (all)	0	1	8
Rash pustular			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 281 (0.36%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	6 / 281 (2.14%)
occurrences (all)	0	0	8

Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	8 / 281 (2.85%)
occurrences (all)	0	0	9
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	11 / 281 (3.91%)
occurrences (all)	0	1	11
Decreased appetite			
subjects affected / exposed	8 / 13 (61.54%)	2 / 10 (20.00%)	39 / 281 (13.88%)
occurrences (all)	12	2	49
Hyponatraemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	7 / 281 (2.49%)
occurrences (all)	1	0	7
Hypomagnesaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	4 / 281 (1.42%)
occurrences (all)	0	0	6
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	14 / 281 (4.98%)
occurrences (all)	0	4	19
Hypoalbuminaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	11 / 281 (3.91%)
occurrences (all)	0	1	11
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 281 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Part 2: Pembrolizumab + Chemotherapy (First Course)	Part 2: Pembrolizumab + Chemotherapy (Second Course)	Part 1: Pembrolizumab + Gemcitabine/Carboplatin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	551 / 562 (98.04%)	11 / 12 (91.67%)	11 / 11 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Flushing			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	22	0	0

Deep vein thrombosis			
subjects affected / exposed	9 / 562 (1.60%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	10	1	0
Hypotension			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	11	0	0
Hot flush			
subjects affected / exposed	21 / 562 (3.74%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	22	0	0
Lymphoedema			
subjects affected / exposed	16 / 562 (2.85%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	17	0	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Infusion site pain			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infusion site extravasation			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Fatigue			
subjects affected / exposed	180 / 562 (32.03%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	258	1	1
Chills			
subjects affected / exposed	16 / 562 (2.85%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	18	1	0
Chest pain			
subjects affected / exposed	25 / 562 (4.45%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	27	0	0
Asthenia			
subjects affected / exposed	108 / 562 (19.22%)	0 / 12 (0.00%)	3 / 11 (27.27%)
occurrences (all)	194	0	6
Thirst			

subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	65 / 562 (11.57%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	83	0	0
Oedema			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Mucosal inflammation			
subjects affected / exposed	31 / 562 (5.52%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	41	0	0
Mucosal dryness			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	25 / 562 (4.45%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	38	0	3
Pyrexia			
subjects affected / exposed	99 / 562 (17.62%)	2 / 12 (16.67%)	2 / 11 (18.18%)
occurrences (all)	150	2	5
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	3 / 562 (0.53%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	4	1	0
Hypersensitivity			
subjects affected / exposed	8 / 562 (1.42%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	9	2	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	24 / 562 (4.27%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	29	0	1
Female genital tract fistula			

subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Bronchostenosis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	118 / 562 (21.00%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	154	0	2
Epistaxis			
subjects affected / exposed	20 / 562 (3.56%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	26	0	0
Haemoptysis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Hydrothorax			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	1 / 562 (0.18%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Nasal pruritus			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	29 / 562 (5.16%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	32	0	1
Pneumothorax			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Productive cough			

subjects affected / exposed	12 / 562 (2.14%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	12	0	0
Pulmonary embolism			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Sinus congestion			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	22 / 562 (3.91%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	23	1	0
Dyspnoea			
subjects affected / exposed	69 / 562 (12.28%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	82	0	1
Dyspnoea exertional			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Throat irritation			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	4	0	1
Anxiety			
subjects affected / exposed	23 / 562 (4.09%)	0 / 12 (0.00%)	3 / 11 (27.27%)
occurrences (all)	23	0	4
Stress			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Persistent depressive disorder			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	48 / 562 (8.54%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	53	0	2

Depression			
subjects affected / exposed	20 / 562 (3.56%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	20	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	139 / 562 (24.73%)	2 / 12 (16.67%)	2 / 11 (18.18%)
occurrences (all)	242	2	28
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Amylase increased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	131 / 562 (23.31%)	1 / 12 (8.33%)	2 / 11 (18.18%)
occurrences (all)	225	1	17
Blood alkaline phosphatase increased			
subjects affected / exposed	50 / 562 (8.90%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	79	1	0
Blood cholesterol increased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	3
Blood corticotrophin increased			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood iron decreased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	31 / 562 (5.52%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	34	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	10 / 562 (1.78%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	10	0	0

Cortisol decreased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	20 / 562 (3.56%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	35	0	2
Haemoglobin decreased			
subjects affected / exposed	14 / 562 (2.49%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	19	0	3
Lipase increased			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	30 / 562 (5.34%)	2 / 12 (16.67%)	1 / 11 (9.09%)
occurrences (all)	88	17	1
Weight increased			
subjects affected / exposed	14 / 562 (2.49%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	14	0	2
White blood cell count decreased			
subjects affected / exposed	106 / 562 (18.86%)	4 / 12 (33.33%)	2 / 11 (18.18%)
occurrences (all)	502	29	3
Weight decreased			
subjects affected / exposed	50 / 562 (8.90%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	55	0	1
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	38
Neutrophil count decreased			
subjects affected / exposed	128 / 562 (22.78%)	4 / 12 (33.33%)	1 / 11 (9.09%)
occurrences (all)	668	29	1
Neutrophil percentage decreased			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	24	0	0
Platelet count decreased			

subjects affected / exposed	87 / 562 (15.48%)	2 / 12 (16.67%)	0 / 11 (0.00%)
occurrences (all)	350	10	0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Incision site pain			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Fracture			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Contusion			
subjects affected / exposed	9 / 562 (1.60%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	10	0	1
Wound complication			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	4	0	2
Animal bite			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	11	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	111 / 562 (19.75%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	184	1	1
Dysgeusia			
subjects affected / exposed	54 / 562 (9.61%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	63	0	0
Dizziness			

subjects affected / exposed	52 / 562 (9.25%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	61	0	0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	15	0	1
Mental impairment			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Somnolence			
subjects affected / exposed	9 / 562 (1.60%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Presyncope			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Polyneuropathy			
subjects affected / exposed	12 / 562 (2.14%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	12	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	49 / 562 (8.72%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	55	0	2
Peripheral motor neuropathy			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Paraesthesia			
subjects affected / exposed	24 / 562 (4.27%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	31	0	0
Neurotoxicity			

subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Neuropathy peripheral			
subjects affected / exposed	62 / 562 (11.03%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	72	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	294 / 562 (52.31%)	4 / 12 (33.33%)	8 / 11 (72.73%)
occurrences (all)	633	22	12
Thrombocytopenia			
subjects affected / exposed	110 / 562 (19.57%)	0 / 12 (0.00%)	5 / 11 (45.45%)
occurrences (all)	346	0	89
Neutropenia			
subjects affected / exposed	232 / 562 (41.28%)	2 / 12 (16.67%)	7 / 11 (63.64%)
occurrences (all)	936	4	90
Lymphopenia			
subjects affected / exposed	30 / 562 (5.34%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	62	0	0
Leukopenia			
subjects affected / exposed	111 / 562 (19.75%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	461	0	64
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	20 / 562 (3.56%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	22	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	20 / 562 (3.56%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	20	0	1
Eye pain			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Eye swelling			

subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Eyelid cyst			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	9 / 562 (1.60%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	11	0	1
Eye pruritus			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	2
Diarrhoea			
subjects affected / exposed	155 / 562 (27.58%)	1 / 12 (8.33%)	6 / 11 (54.55%)
occurrences (all)	305	2	6
Dental caries			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Constipation			
subjects affected / exposed	155 / 562 (27.58%)	0 / 12 (0.00%)	6 / 11 (54.55%)
occurrences (all)	212	0	10
Colitis			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Anal fissure			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Abdominal pain upper			
subjects affected / exposed	45 / 562 (8.01%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	64	1	1

Abdominal pain			
subjects affected / exposed	43 / 562 (7.65%)	0 / 12 (0.00%)	3 / 11 (27.27%)
occurrences (all)	57	0	6
Abdominal distension			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	13	0	1
Dry mouth			
subjects affected / exposed	22 / 562 (3.91%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	23	0	0
Gastritis			
subjects affected / exposed	18 / 562 (3.20%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	18	3	0
Flatulence			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	13	0	1
Dyspepsia			
subjects affected / exposed	38 / 562 (6.76%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	45	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	15 / 562 (2.67%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	16	0	1
Gingival bleeding			
subjects affected / exposed	3 / 562 (0.53%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Vomiting			
subjects affected / exposed	140 / 562 (24.91%)	0 / 12 (0.00%)	6 / 11 (54.55%)
occurrences (all)	248	0	8
Stomatitis			
subjects affected / exposed	54 / 562 (9.61%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	76	0	0
Nausea			
subjects affected / exposed	251 / 562 (44.66%)	1 / 12 (8.33%)	4 / 11 (36.36%)
occurrences (all)	522	1	9
Large intestinal haemorrhage			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Hepatic function abnormal			
subjects affected / exposed	5 / 562 (0.89%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	6	1	0
Skin and subcutaneous tissue disorders			
Butterfly rash			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	190 / 562 (33.81%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	194	0	2
Dermatitis acneiform			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	11	0	3
Dermatitis contact			
subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	8	0	1
Nail discolouration			
subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Dry skin			
subjects affected / exposed	16 / 562 (2.85%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	18	0	1
Dyshidrotic eczema			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Erythema			
subjects affected / exposed	23 / 562 (4.09%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	25	0	0
Erythema nodosum			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hyperhidrosis			

subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Drug eruption			
subjects affected / exposed	2 / 562 (0.36%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Onychalgia			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Nail dystrophy			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pigmentation disorder			
subjects affected / exposed	1 / 562 (0.18%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Skin mass			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Skin lesion			
subjects affected / exposed	4 / 562 (0.71%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	5	1	0
Skin hyperpigmentation			
subjects affected / exposed	7 / 562 (1.25%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Rash pruritic			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	7	0	1
Rash papular			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Rash maculo-papular			
subjects affected / exposed	25 / 562 (4.45%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	41	0	0

Pruritus			
subjects affected / exposed	85 / 562 (15.12%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	120	1	1
Rash			
subjects affected / exposed	110 / 562 (19.57%)	0 / 12 (0.00%)	3 / 11 (27.27%)
occurrences (all)	154	0	4
Urticaria			
subjects affected / exposed	11 / 562 (1.96%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	15	0	1
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 562 (0.18%)	2 / 12 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Dysuria			
subjects affected / exposed	12 / 562 (2.14%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	12	0	0
Polyuria			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	25 / 562 (4.45%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	25	0	1
Adrenal insufficiency			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Hypophysitis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	85 / 562 (15.12%)	0 / 12 (0.00%)	4 / 11 (36.36%)
occurrences (all)	96	0	5
Thyroiditis			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Musculoskeletal and connective tissue disorders			

Groin pain			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Joint swelling			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	2
Coccydynia			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	22 / 562 (3.91%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	25	0	0
Back pain			
subjects affected / exposed	72 / 562 (12.81%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	88	2	1
Arthritis			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	8	0	0
Arthralgia			
subjects affected / exposed	122 / 562 (21.71%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	203	0	3
Musculoskeletal chest pain			
subjects affected / exposed	28 / 562 (4.98%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	31	0	0
Spinal pain			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	5	0	2
Pain in jaw			
subjects affected / exposed	10 / 562 (1.78%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	11	0	0
Pain in extremity			
subjects affected / exposed	56 / 562 (9.96%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	68	1	0
Osteoporosis			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1

Neck pain			
subjects affected / exposed	25 / 562 (4.45%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	28	0	1
Myalgia			
subjects affected / exposed	59 / 562 (10.50%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	83	0	3
Musculoskeletal stiffness			
subjects affected / exposed	3 / 562 (0.53%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Synovial cyst			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	28 / 562 (4.98%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	30	0	2
Lip infection			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	53 / 562 (9.43%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	76	1	1
Appendicitis			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
COVID-19			

subjects affected / exposed	2 / 562 (0.36%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Cellulitis			
subjects affected / exposed	9 / 562 (1.60%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Conjunctivitis			
subjects affected / exposed	7 / 562 (1.25%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	9	1	1
Conjunctivitis viral			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	11 / 562 (1.96%)	1 / 12 (8.33%)	2 / 11 (18.18%)
occurrences (all)	13	1	2
Erythema infectiosum			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	6	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 562 (0.18%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Vulvovaginitis			
subjects affected / exposed	0 / 562 (0.00%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Viral infection			
subjects affected / exposed	9 / 562 (1.60%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	14	1	0
Viral diarrhoea			
subjects affected / exposed	0 / 562 (0.00%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urinary tract infection			

subjects affected / exposed	49 / 562 (8.72%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	70	1	1
Upper respiratory tract infection			
subjects affected / exposed	58 / 562 (10.32%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	94	0	9
Tonsillitis			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	9	0	1
Skin infection			
subjects affected / exposed	6 / 562 (1.07%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Pharyngitis			
subjects affected / exposed	8 / 562 (1.42%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	8	0	0
Rash pustular			
subjects affected / exposed	4 / 562 (0.71%)	0 / 12 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Rhinitis			
subjects affected / exposed	5 / 562 (0.89%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	5	0	1
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	9 / 562 (1.60%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	13	0	48
Hyperglycaemia			
subjects affected / exposed	27 / 562 (4.80%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	40	1	4
Decreased appetite			
subjects affected / exposed	118 / 562 (21.00%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	140	0	4
Hyponatraemia			
subjects affected / exposed	12 / 562 (2.14%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	14	0	1
Hypomagnesaemia			
subjects affected / exposed	15 / 562 (2.67%)	1 / 12 (8.33%)	0 / 11 (0.00%)
occurrences (all)	23	1	0

Hypokalaemia			
subjects affected / exposed	28 / 562 (4.98%)	1 / 12 (8.33%)	1 / 11 (9.09%)
occurrences (all)	46	1	2
Hypoalbuminaemia			
subjects affected / exposed	18 / 562 (3.20%)	0 / 12 (0.00%)	2 / 11 (18.18%)
occurrences (all)	28	0	28
Hypoglycaemia			
subjects affected / exposed	2 / 562 (0.36%)	0 / 12 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2016	AM 1: Change in pneumonitis exclusion criteria
13 March 2018	AM 2: guidelines were added for dose modification in the event of myocarditis and updated guidelines for several other conditions.
07 September 2018	AM 3: Change in testing of primary endpoints at interim analysis 1
11 April 2019	AM 4: Change in timing of final analysis
14 October 2019	AM 5: The objectives, hypotheses, and statistical analysis plan were changed to include subjects with PD-L1 positive tumors with a higher combined positive score (CPS) cutoff of ≥10 (CPS ≥10).
27 October 2021	AM 6: To include language pertaining to the KN587 extension trial, as the plan is to transition current subjects over to KN587.
12 July 2022	Sponsor name and address change

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported