Clinical trial results:
A Randomized, Multicenter, Double-Blind, Phase 3 Study of Nivolumab, Nivolumab in Combination With Ipilimumab, or Placebo as Maintenance Therapy in Subjects With Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) After Completion of Platinum-based First Line Chemotherapy (CheckMate 451: CHECKpoint Pathway and nivoluMAb Clinical Trial Evaluation 451)

Summary

EudraCT number	2015-002441-61
Trial protocol	BE AT GR SE DE ES GB IE FI PL NL RO
Global end of trial date	11 November 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	CA209-451

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02538666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Bristol-Myers Squibb, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	20 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if nivolumab or nivolumab in combination with ipilimumab improve Overall Survival (OS) versus placebo in participants with Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) who have completed a first line platinum-based chemotherapy regimen and achieved an ongoing Complete Response (CR), Partial Response (PR) or Stable Disease (SD).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Brazil: 50
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	China: 77
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 46
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Ireland: 16
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 84
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Netherlands: 8

Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Korea, Republic of: 85
Country: Number of subjects enrolled	Romania: 40
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	Spain: 49
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Switzerland: 18
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 159
Worldwide total number of subjects	909
EEA total number of subjects	292

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)	463
From 65 to 84 years	445
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

907 participants were randomized and 903 were treated. 2 participants were concurrently participating in both the Global and China population. These participants also contributed data to both the Global and China population.

Pre-assignment

Screening details:

The global study population is defined as all participants enrolled during the global accrual window, including any patient from China enrolled in the window. The China population is defined as all participants from China enrolled in the study, including any subject from China enrolled in the global study as well as the China sub-study.

Period 1

Period 1 title	Pre-Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Global Placebo

Arm description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Arm type	Placebo
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Placebo for nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Arm title	Global Nivolumab 240 mg

Arm description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Arm type	Experimental
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg was administered every 2 weeks as a 30-minute IV infusion

Arm title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg was administered as a 90-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 1 mg/kg was administered as a 30-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm title	China Placebo

Arm description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Arm type	Placebo
Investigational medicinal product name	Placebo for nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Arm title	China Nivolumab 240 mg

Arm description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Arm type	Experimental
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg was administered every 2 weeks as a 30-minute IV infusion

Arm title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg was administered as a 90-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 1 mg/kg was administered as a 30-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Number of subjects in period 1	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Started	275	280	279
Completed	273	279	278
Not completed	2	1	1
Withdrew Consent	-	1	1
Disease progression	1	-	-
no longer meets study criteria	1	-	-

Number of subjects in period 1	China Placebo	China Nivolumab 240 mg	China Nivolumab 1 mg/kg + Ipilimumab

			3 mg/kg
Started	26	25	24
Completed	26	25	24
Not completed	0	0	0
Withdrew Consent	-	-	-
Disease progression	-	-	-
no longer meets study criteria	-	-	-

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Global Placebo

Arm description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Arm type	Placebo
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Placebo for nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Arm title	Global Nivolumab 240 mg

Arm description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Arm type	Experimental
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg was administered every 2 weeks as a 30-minute IV infusion

Arm title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 1 mg/kg was administered as a 30-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg was administered as a 90-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm title	China Placebo

Arm description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Arm type	Placebo
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Placebo for nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Arm title	China Nivolumab 240 mg

Arm description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Arm type	Experimental
Investigational medicinal product name	Placebo for ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose was administered as an IV infusion

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg was administered every 2 weeks as a 30-minute IV infusion

Arm title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg was administered as a 90-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 1 mg/kg was administered as a 30-minute IV infusion every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Number of subjects in period 2	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Started	273	279	278
Completed	0	0	0
Not completed	273	279	278
Adverse event, serious fatal	-	2	2
Disease progression	248	209	150
Participant withdrew consent	1	5	2
Maximum clinical benefit	4	2	4
Participant no longer meets study criteria	-	2	-

Other reasons	8	14	5
Study drug toxicity	1	25	88
Not reported	1	2	1
Adverse event unrelated to study drug	8	10	15
Lost to follow-up	-	1	1
Poor/non-compliance	-	1	-
Participant request to discontinue study treatment	2	6	9
Administrative reason by sponsor	-	-	1

Number of subjects in period 2	China Placebo	China Nivolumab 240 mg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Started	26	25	24
Completed	0	0	0
Not completed	26	25	24
Adverse event, serious fatal	-	-	1
Disease progression	23	18	15
Participant withdrew consent	1	-	1
Maximum clinical benefit	-	1	-
Participant no longer meets study criteria	-	-	-
Other reasons	-	1	-
Study drug toxicity	-	5	4
Not reported	1	-	1
Adverse event unrelated to study drug	-	-	-
Lost to follow-up	-	-	-
Poor/non-compliance	-	-	-
Participant request to discontinue study treatment	1	-	2
Administrative reason by sponsor	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Global Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	Global Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	
Reporting group title	China Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	China Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	

Reporting group values	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects	275	280	279
Age Categorical Units:			
< 65	148	135	140
≥ 65 and < 75	103	110	103
≥ 75 and < 85	24	35	35
≥ 85	0	0	1
Sex: Female, Male Units: Participants			
Female	100	103	99
Male	175	177	180
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	14	11	15
Not Hispanic or Latino	151	159	164
Unknown or Not Reported	110	110	100
Race/Ethnicity, Customized Units: Subjects			
Asian	69	58	58
Black or African American	2	6	1
White	198	213	216
Other	6	3	3

Not Reported	0	0	1

Reporting group values	China Placebo	China Nivolumab 240 mg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects	26	25	24
Age Categorical Units:			
< 65	14	14	12
≥ 65 and < 75	10	11	12
≥ 75 and < 85	2	0	0
≥ 85	0	0	0
Sex: Female, Male Units: Participants			
Female	3	3	2
Male	23	22	22
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	10	5	7
Unknown or Not Reported	16	20	17
Race/Ethnicity, Customized Units: Subjects			
Asian	26	25	24
Black or African American	0	0	0
White	0	0	0
Other	0	0	0
Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	909		
Age Categorical Units:			
< 65	463		
≥ 65 and < 75	349		
≥ 75 and < 85	96		
≥ 85	1		
Sex: Female, Male Units: Participants			
Female	310		
Male	599		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	40		
Not Hispanic or Latino	496		
Unknown or Not Reported	373		
Race/Ethnicity, Customized Units: Subjects			
Asian	260		
Black or African American	9		

White	627		
Other	12		
Not Reported	1		

End points

End points reporting groups

Reporting group title	Global Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	Global Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	
Reporting group title	China Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	China Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	
Reporting group title	Global Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	Global Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	
Reporting group title	China Placebo
Reporting group description:	
100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion	
Reporting group title	China Nivolumab 240 mg
Reporting group description:	
Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion	
Reporting group title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description:	
Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks	

Primary: Overall Survival (OS) of Nivolumab + Ipilimumab Versus Placebo In The Global Population

End point title	Overall Survival (OS) of Nivolumab + Ipilimumab Versus Placebo In The Global Population[1]

End point description:

OS was defined as the time from randomization to the date of death. A participant who had not died was censored at last known alive date. OS was followed up during the blinded study drug treatment and every 3 months via in-person or phone contact after participant discontinued the blinded study drug

End point type	Primary

End point timeframe:

From randomization to 400 deaths across the two treatment groups (Nivo+Ipi vs Placebo) (up to approximately 37 months)

Notes:

[1] - 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Placebo	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	279		
Units: Months				
median (confidence interval 95%)	9.56 (8.18 to 11.01)	9.17 (8.15 to 10.25)		

Statistical analyses

Statistical analysis title	nivolumab + ipilimumab over placebo

Statistical analysis description:

nivolumab + ipilimumab over placebo

Comparison groups	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg v Global Placebo
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3693
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.12

Secondary: Overall Survival (OS) of Nivolumab Versus Placebo

End point title	Overall Survival (OS) of Nivolumab Versus Placebo[2]

End point description:

Overall Survival (OS) comparing nivolumab monotherapy versus placebo. OS was defined as the time from randomization to the date of death. A participant who had not died was censored at last known alive date. OS was followed up during the blinded study drug treatment and every 3 months via in-person or phone contact after participant discontinued the blinded study drug.

End point type	Secondary

End point timeframe:

From randomization to the date of death or last known alive date (up to approximately 73 months)

Notes:

[2] - 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Placebo	Global Nivolumab 240 mg	China Placebo	China Nivolumab 240 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	275	280	26	25
Units: Months				
median (confidence interval 95%)	9.56 (8.18 to 11.01)	10.18 (9.43 to 11.99)	9.28 (5.59 to 14.26)	8.18 (7.20 to 14.26)

Statistical analyses

Statistical analysis title	Global nivolumab over global placebo
Statistical analysis description:	
Global nivolumab over global placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	555
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.97

Statistical analysis title	China nivolumab over China Placebo
Statistical analysis description:	
China nivolumab over China Placebo	
Comparison groups	China Placebo v China Nivolumab 240 mg

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.66

Secondary: Overall Survival (OS) of Nivolumab + Ipilimumab Versus Nivolumab

End point title	Overall Survival (OS) of Nivolumab + Ipilimumab Versus Nivolumab[3]

End point description:

Overall Survival (OS) comparing Nivolumab + Ipilimumab Versus Nivolumab. OS was defined as the time from randomization to the date of death. A participant who had not died was censored at last known alive date. OS was followed up during the blinded study drug treatment and every 3 months via in-person or phone contact after participant discontinued the blinded study drug.

End point type	Secondary

End point timeframe:

From randomization to the date of death or last known alive date (up to approximately 73 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	China Nivolumab 240 mg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	280	279	25	24
Units: Months				
median (confidence interval 95%)	10.18 (9.43 to 11.99)	9.17 (8.15 to 10.35)	8.18 (7.20 to 14.26)	10.48 (7.13 to 13.40)

Statistical analyses

Statistical analysis title	Global nivo + ipi over global nivo

Statistical analysis description:

Global nivolumab + ipilimumab over global nivolumab

Comparison groups	Global Nivolumab 240 mg v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.36

Statistical analysis title	China nivolumab + ipilimumab over China nivolumab
Statistical analysis description:	
China nivolumab + ipilimumab over China nivolumab	
Comparison groups	China Nivolumab 240 mg v China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.79

Secondary: Progression Free Survival (PFS) per BICR

End point title	Progression Free Survival (PFS) per BICR

End point description:

PFS was defined as the time between the date of randomization and the first date of documented progression as determined by Blind Independent Central Review (BICR) or death due to any cause, whichever occurred first. Participants who died with no reported progression were considered to have progressed on the date of death. Participants who did not progress or die were censored on the date of their last evaluable tumor assessment on or prior to initiation of the subsequent anti-cancer therapy. Participants who did not have any on study tumor assessments and did not die (or died after initiation of the subsequent anti- cancer therapy) were censored on their date of randomization. Participants who started any subsequent anti- cancer therapy without a prior reported Progressive Disease (PD) per BICR were censored at the last evaluable tumor assessment on or prior to initiation of the subsequent anti-cancer therapy.

End point type	Secondary

End point timeframe:

From randomization to the date of the first documented tumor progression or death due to any cause (up to approximately 73 months)

End point values	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	China Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	275	280	279	26
Units: Months				
median (confidence interval 95%)	1.41 (1.41 to 1.48)	1.94 (1.61 to 2.63)	1.74 (1.48 to 2.63)	1.38 (1.28 to 2.56)

End point values	China Nivolumab 240 mg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Months				
median (confidence interval 95%)	1.58 (1.38 to 4.11)	1.54 (1.28 to 2.73)		

Statistical analyses

Statistical analysis title	Global nivolumab + ipilimumab over global placebo
Statistical analysis description: Global nivolumab + ipilimumab over global placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.88

Statistical analysis title	Global nivolumab over global placebo
Statistical analysis description: Global nivolumab over global placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg

Number of subjects included in analysis	555
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.79

Statistical analysis title	Global nivolumab+ ipilimumab over nivolumab
Statistical analysis description:	
Global nivolumab+ ipilimumab over nivolumab	
Comparison groups	Global Nivolumab 240 mg v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.35

Statistical analysis title	China Nivolumab + Ipilimumab over China placebo
Statistical analysis description:	
China Nivolumab + Ipilimumab over China placebo	
Comparison groups	China Placebo v China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.12

Statistical analysis title	China Nivolumab over China placebo

Statistical analysis description:	
China Nivolumab over China placebo	
Comparison groups	China Placebo v China Nivolumab 240 mg
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.85

Statistical analysis title	China Nivolumab + Ipilimumab over China Nivolumab
Statistical analysis description:	
China Nivolumab + Ipilimumab over China Nivolumab	
Comparison groups	China Nivolumab 240 mg v China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.49

Secondary: Overall Survival (OS) in Tumor Mutational Burden (TMB) High and Low Subgroups by TMB Cutoff In The Global Population

End point title	Overall Survival (OS) in Tumor Mutational Burden (TMB) High and Low Subgroups by TMB Cutoff In The Global Population[4]

End point description:

Tumor mutational burden (TMB) is measured using FoundationOne CDxTM (F1CDx) assay, a comprehensive genomic profile (CGP) assay based on baseline tumor tissue. TMB is defined as the number of somatic, coding, base substitution, and indel mutations per megabase of genome examined.

OS in TMB by the following cutoff points: ≥10 mutations/mb, < 10 mutations/mb, ≥13 mutations/mb, <13 mutations/mb

End point type	Secondary

End point timeframe:

From randomization to the date of death or last known alive date (up to approximately 73 months)

Notes:

[4] - 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	196	192	
Units: Months				
median (confidence interval 95%)				
≥10 mutations/mb	11.96 (7.49 to 13.67)	12.81 (9.95 to 18.60)	10.55 (8.38 to 14.16)	
< 10 mutations/mb	9.20 (7.46 to 11.04)	9.76 (8.34 to 11.30)	8.11 (6.60 to 10.05)	
≥13 mutations/mb	9.69 (6.21 to 13.63)	12.98 (9.95 to 18.60)	13.47 (9.26 to 21.75)	
<13 mutations/mb	10.02 (7.66 to 11.47)	9.89 (8.64 to 11.30)	7.85 (6.67 to 9.66)	

Statistical analyses

Statistical analysis title	TMB cutoff ≥10 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description: TMB cutoff ≥10 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.15

Statistical analysis title	TMB cutoff ≥10 mutations/mb: Nivo over placebo
Statistical analysis description: TMB cutoff ≥10 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.04

Statistical analysis title	TMB cutoff ≥13 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff ≥13 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.92

Statistical analysis title	TMB cutoff ≥13 mutations/mb: Nivo over placebo
Statistical analysis description:	
TMB cutoff ≥13 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.93

Statistical analysis title	TMB cutoff <10 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff <10 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.21

Statistical analysis title	TMB cutoff <10 mutations/mb: Nivo over placebo
Statistical analysis description:	
TMB cutoff <10 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.18

Statistical analysis title	TMB cutoff <13 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff <13 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.35

Statistical analysis title	TMB cutoff <13 mutations/mb: Nivo over placebo

Statistical analysis description:	
TMB cutoff <13 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.2

Secondary: Progression Free Survival (PFS) per BICR in Tumor Mutational Burden (TMB) High and Low Subgroups by TMB Cutoff In The Global Population

End point title	Progression Free Survival (PFS) per BICR in Tumor Mutational Burden (TMB) High and Low Subgroups by TMB Cutoff In The Global Population[5]

End point description:

Tumor mutational burden (TMB) is measured using FoundationOne CDxTM (F1CDx) assay, a comprehensive genomic profile (CGP) assay based on baseline tumor tissue. TMB is defined as the number of somatic, coding, base substitution, and indel mutations per megabase of genome examined.

PFS in TMB by the following cutoff points: ≥10 mutations/mb, < 10 mutations/mb, ≥13 mutations/mb, <13 mutations/mb.

End point type	Secondary

End point timeframe:

From randomization to the date of the first documented tumor progression or death due to any cause (up to approximately 73 months)

Notes:

[5] - 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Placebo	Global Nivolumab 240 mg	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	192	196	192	
Units: Months				
median (confidence interval 95%)				
≥10 mutations/mb	1.58 (1.41 to 2.63)	2.79 (2.04 to 4.17)	2.33 (1.48 to 2.92)	
< 10 mutations/mb	1.41 (1.35 to 1.45)	1.61 (1.45 to 2.53)	1.48 (1.41 to 2.00)	
≥13 mutations/mb	1.58 (1.41 to 2.63)	2.76 (1.61 to 4.11)	2.63 (1.48 to 3.81)	
<13 mutations/mb	1.41 (1.38 to 1.45)	1.84 (1.48 to 2.66)	1.48 (1.41 to 2.00)	

Statistical analyses

Statistical analysis title	TMB cutoff ≥10 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff ≥10 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.09

Statistical analysis title	TMB cutoff ≥13 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff ≥13 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.07

Statistical analysis title	TMB cutoff ≥10 mutations/mb: Nivo over placebo
Statistical analysis description:	
TMB cutoff ≥10 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg

Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.92

Statistical analysis title	TMB cutoff ≥13 mutations/mb: Nivo over placebo
Statistical analysis description:	
TMB cutoff ≥13 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.95

Statistical analysis title	TMB cutoff <10 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description:	
TMB cutoff <10 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.96

Statistical analysis title	TMB cutoff <10 mutations/mb: Nivo over placebo

Statistical analysis description: TMB cutoff <10 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.89

Statistical analysis title	TMB cutoff <13 mutations/mb: Nivo+Ipi over placebo
Statistical analysis description: TMB cutoff <13 mutations/mb: Nivo+Ipi over placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.01

Statistical analysis title	TMB cutoff <13 mutations/mb: Nivo over placebo
Statistical analysis description: TMB cutoff <13 mutations/mb: Nivo over placebo	
Comparison groups	Global Placebo v Global Nivolumab 240 mg
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.89

Post-hoc: Overall Survival (OS) of Nivolumab + Ipilimumab Versus Placebo - Extended Collection

End point title	Overall Survival (OS) of Nivolumab + Ipilimumab Versus Placebo - Extended Collection[6]

End point description:

Overall survival (OS) comparing nivolumab + ipilimumab versus placebo. OS was defined as the time from randomization to the date of death. A participant who had not died was censored at last known alive date. OS was followed up during the blinded study drug treatment and every 3 months via in-person or phone contact after participant discontinued the blinded study drug.

Note: This outcome measure represents an updated version of the primary endpoint to include additional data collection that has occurred after the primary completion date. (Assessments were made until 20-Dec-2021).

End point type	Post-hoc

End point timeframe:

From randomization to the date of death or last known alive date (up to approximately 73 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: Endpoints are cohort specific and do not report for all arms.

End point values	Global Placebo	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	China Placebo	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	275	279	26	24
Units: Months				
median (confidence interval 95%)	9.56 (8.18 to 11.01)	9.17 (8.15 to 10.35)	9.28 (5.59 to 14.26)	10.48 (7.13 to 13.40)

Statistical analyses

Statistical analysis title	China nivolumab + ipilimumab over China placebo

Statistical analysis description:

China nivolumab + ipilimumab over China placebo

Comparison groups	China Placebo v China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	50
Analysis specification	Post-hoc
Analysis type	superiority
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.67

Statistical analysis title	Global nivolumab + ipilimumab over Global placebo
Statistical analysis description: Global nivolumab + ipilimumab over Global placebo	
Comparison groups	Global Placebo v Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Number of subjects included in analysis	554
Analysis specification	Post-hoc
Analysis type	superiority
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.09

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from randomization until study completion (up to approximately 73 months). SAEs and Other AEs were assessed from first dose to 100 days after last dose of study therapy (up to approximately 34 months).

Adverse event reporting additional description:

The total number at risk for all-cause mortality represents all participants who were randomized. The total number at risk by any serious adverse event and other (not including serious) adverse events represents all participants that received at least 1 dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Global Placebo

Reporting group description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Reporting group title	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Reporting group title	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Nivolumab 1 mg/kg (30-minute IV infusion) + Ipilimumab 3 mg/kg (90-minute IV infusion) administered every 3 weeks for 4 doses, followed by nivolumab 240 mg every 2 weeks

Reporting group title	China Placebo

Reporting group description:

100 mL of 0.9% Sodium Chloride Solution or 5% Dextrose administered as placebo for nivolumab and ipilimumab as an IV infusion

Reporting group title	China Nivolumab 240 mg

Reporting group description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Reporting group title	Global Nivolumab 240 mg

Reporting group description:

Nivolumab 240 mg administered every 2 weeks as a 30-minute IV infusion

Serious adverse events	Global Placebo	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	117 / 273 (42.86%)	198 / 278 (71.22%)	19 / 24 (79.17%)
number of deaths (all causes)	250	240	23
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Cancer pain			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Malignant neoplasm progression			
subjects affected / exposed	50 / 273 (18.32%)	51 / 278 (18.35%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 52	0 / 53	0 / 2
deaths causally related to treatment / all	0 / 43	0 / 44	0 / 0
Metastases to central nervous system			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Metastases to spinal cord			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Neoplasm progression			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Small cell lung cancer			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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	2 / 273 (0.73%)	0 / 278 (0.00%)	0 / 24 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Embolism			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Hypertension			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Hypotension			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Shock			

subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Superior vena cava stenosis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Superior vena cava syndrome			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Venous thrombosis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 273 (1.10%)	6 / 278 (2.16%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 4	3 / 6	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Chest pain			
subjects affected / exposed	2 / 273 (0.73%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 273 (0.00%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Facial pain			

subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Fatigue			
subjects affected / exposed	2 / 273 (0.73%)	7 / 278 (2.52%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 273 (0.37%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Mucosal inflammation			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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	2 / 273 (0.73%)	0 / 278 (0.00%)	0 / 24 (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
Pain			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Performance status decreased			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pyrexia			

subjects affected / exposed	4 / 273 (1.47%)	8 / 278 (2.88%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 4	5 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Asphyxia			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Atelectasis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 lung disease			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Bronchial haemorrhage			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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

Bronchospasm			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Cough			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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	5 / 273 (1.83%)	4 / 278 (1.44%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Haemoptysis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Hypersensitivity pneumonitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Immune-mediated lung disease			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Interstitial lung disease			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pleural effusion			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pleurisy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pneumonitis			
subjects affected / exposed	2 / 273 (0.73%)	14 / 278 (5.04%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	2 / 2	14 / 14	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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 embolism			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Delirium			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Insomnia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Mental status changes			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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			
Amylase increased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 glucose increased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 physical condition abnormal			
subjects affected / exposed	3 / 273 (1.10%)	0 / 278 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Hepatic enzyme increased			

subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Platelet count decreased			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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			
Craniocerebral injury			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Fall			
subjects affected / exposed	2 / 273 (0.73%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Femur fracture			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Fracture			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Hip fracture			
subjects affected / exposed	2 / 273 (0.73%)	0 / 278 (0.00%)	0 / 24 (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
Infusion related reaction			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Radiation pneumonitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Spinal compression fracture			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Tendon rupture			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Angina unstable			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 / 273 (0.00%)	2 / 278 (0.72%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Cardiac failure			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Coronary artery disease			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Myocardial infarction			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 tachycardia			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 infarction			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Cognitive disorder			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Dizziness			

subjects affected / exposed	2 / 273 (0.73%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Encephalitis autoimmune			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Guillain-Barre syndrome			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Hemiparesis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Immune-mediated encephalitis			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lethargy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Limbic encephalitis			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Myasthenia gravis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Myelopathy			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Neurological decompensation			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Neurological symptom			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Occipital neuralgia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Paraesthesia			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Paraparesis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Partial seizures			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Peripheral motor neuropathy			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Seizure			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Spinal cord compression			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Status epilepticus			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Syncope			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Tremor			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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			
Anaemia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Febrile neutropenia			
subjects affected / exposed	7 / 273 (2.56%)	7 / 278 (2.52%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 7	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune thrombocytopenia			

subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 273 (0.37%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Eyelid ptosis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Iridocyclitis			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Papilloedema			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Vision blurred			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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			
Abdominal pain			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Colitis			
subjects affected / exposed	0 / 273 (0.00%)	19 / 278 (6.83%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	23 / 23	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Colitis ulcerative			

subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Diarrhoea			
subjects affected / exposed	1 / 273 (0.37%)	16 / 278 (5.76%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	17 / 19	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 273 (0.37%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Enterocolitis haemorrhagic			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Enterocutaneous fistula			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haematemesis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Inguinal hernia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Intestinal infarction			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Intestinal obstruction			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Mouth haemorrhage			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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	1 / 273 (0.37%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic mass			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Pancreatitis			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Proctitis ulcerative			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Small intestinal haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Stomatitis			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Vomiting			
subjects affected / exposed	3 / 273 (1.10%)	5 / 278 (1.80%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	3 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Drug-induced liver injury			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatitis			
subjects affected / exposed	0 / 273 (0.00%)	4 / 278 (1.44%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			

subjects affected / exposed	0 / 273 (0.00%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pruritus			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Psoriasis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Rash			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 273 (0.00%)	3 / 278 (1.08%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin toxicity			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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			
Acute kidney injury			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bladder mass			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Immune-mediated cystitis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 273 (0.37%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal tubular disorder			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Endocrine disorders			

Adrenal insufficiency			
subjects affected / exposed	0 / 273 (0.00%)	4 / 278 (1.44%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	5 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Cushing's syndrome			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Hyperthyroidism			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Immune-mediated adrenal insufficiency			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Immune-mediated hyperthyroidism			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed	1 / 273 (0.37%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Mobility decreased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Muscular weakness			
subjects affected / exposed	3 / 273 (1.10%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Myopathy			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Myositis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Osteoporotic fracture			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal disorder			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Spinal pain			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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			
Abdominal abscess			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Anal abscess			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Bacterial diarrhoea			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Bronchitis			
subjects affected / exposed	1 / 273 (0.37%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus enteritis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Diverticulitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Encephalitis			

subjects affected / exposed	0 / 273 (0.00%)	3 / 278 (1.08%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Gastric infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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 infection			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Herpes simplex			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Herpes zoster			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Infective thrombosis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Influenza			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Osteomyelitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Periodontitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Pneumonia			
subjects affected / exposed	9 / 273 (3.30%)	12 / 278 (4.32%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 15	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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 legionella			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Pulmonary sepsis			

subjects affected / exposed	2 / 273 (0.73%)	0 / 278 (0.00%)	0 / 24 (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
Respiratory tract infection			
subjects affected / exposed	1 / 273 (0.37%)	1 / 278 (0.36%)	0 / 24 (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
Sepsis			
subjects affected / exposed	3 / 273 (1.10%)	8 / 278 (2.88%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 5	1 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Septic shock			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Toxic shock syndrome			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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	2 / 273 (0.73%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Decreased appetite			
subjects affected / exposed	2 / 273 (0.73%)	3 / 278 (1.08%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	1 / 2	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 273 (0.73%)	6 / 278 (2.16%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	3 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Electrolyte imbalance			

subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	0 / 24 (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
Failure to thrive			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	0 / 24 (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
Hyperglycaemia			
subjects affected / exposed	1 / 273 (0.37%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (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
Hyponatraemia			
subjects affected / exposed	5 / 273 (1.83%)	9 / 278 (3.24%)	2 / 24 (8.33%)
occurrences causally related to treatment / all	0 / 5	2 / 10	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	China Placebo	China Nivolumab 240 mg	Global Nivolumab 240 mg

Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 26 (30.77%)	10 / 25 (40.00%)	131 / 279 (46.95%)
number of deaths (all causes)	24	23	231
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Lung cancer metastatic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Malignant neoplasm progression			
subjects affected / exposed	4 / 26 (15.38%)	1 / 25 (4.00%)	50 / 279 (17.92%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 52
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 45
Metastases to central nervous system			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Metastases to spinal cord			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Neoplasm progression			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	4 / 279 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Small cell lung cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Tumour pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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			
Circulatory collapse			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Embolism			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Hypertension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Superior vena cava stenosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	4 / 279 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Facial pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	5 / 279 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Influenza like illness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Mucosal inflammation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Performance status decreased			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	3 / 279 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Asphyxia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Atelectasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Autoimmune lung disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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

Bronchial haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Bronchospasm			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 obstructive pulmonary disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	5 / 279 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	9 / 279 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Haemoptysis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hypersensitivity pneumonitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hypoxia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated lung disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Interstitial lung disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Pleural effusion			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	1 / 25 (4.00%)	8 / 279 (2.87%)
occurrences causally related to treatment / all	0 / 0	1 / 1	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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 haemorrhage			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Respiratory failure			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Delirium			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Insomnia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Mental status changes			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Investigations			
Amylase increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Blood glucose increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
General physical condition abnormal			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Lipase increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (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
Platelet count decreased			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 1	2 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
White blood cell count decreased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (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
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (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
Fall			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Femoral neck fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Femur fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hip fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Infusion related reaction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Radiation pneumonitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Spinal compression fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Tendon rupture			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Angina unstable			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 flutter			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Cardiac failure acute			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Cardio-respiratory arrest			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Coronary artery disease			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Myocardial infarction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Myocarditis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Pericardial effusion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	1 / 279 (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
Sinus tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Cauda equina syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Cerebral infarction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Cognitive disorder			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Dizziness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Dysarthria			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Encephalitis autoimmune			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Encephalopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Epilepsy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hemiparesis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated encephalitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Ischaemic stroke			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Lethargy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Limbic encephalitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Myasthenia gravis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Neurological decompensation			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Neurological symptom			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Occipital neuralgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Paraesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Paraparesis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Partial seizures			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 motor neuropathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Seizure			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Spinal cord compression			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Status epilepticus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Syncope			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Tremor			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	3 / 279 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	3 / 279 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune thrombocytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Myelosuppression			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (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
Neutropenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Thrombocytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (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
Eyelid ptosis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Iridocyclitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Papilloedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Rhegmatogenous retinal detachment			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Vision blurred			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Anal fistula			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Colitis ischaemic			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 ulcerative			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Constipation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Dysphagia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Enteritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Enterocolitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Enterocolitis haemorrhagic			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Enterocutaneous fistula			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Impaired gastric emptying			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Inguinal hernia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 infarction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 perforation			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Mouth haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Nausea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic mass			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Pancreatitis acute			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Proctitis ulcerative			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Small intestinal haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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-induced liver injury			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Hepatic failure			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatic function abnormal			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Hepatitis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Immune-mediated hepatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 injury			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Psoriasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 toxicity			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Subcutaneous emphysema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Bladder mass			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated cystitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Renal tubular disorder			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Adrenal insufficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Cushing's syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hyperthyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Hypopituitarism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated adrenal insufficiency			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Immune-mediated hyperthyroidism			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Arthritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Back pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Mobility decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Muscular weakness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Myopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Myositis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Osteoporotic fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Spinal disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Spinal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
Abdominal abscess			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Anal abscess			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Bronchitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Cytomegalovirus enteritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Diverticulitis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Encephalitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gastric infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Herpes simplex			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Herpes zoster			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Infective thrombosis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Influenza			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Neutropenic infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Osteomyelitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Periodontitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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	1 / 26 (3.85%)	0 / 25 (0.00%)	6 / 279 (2.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia aspiration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 legionella			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 sepsis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Toxic shock syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Upper respiratory tract infection			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
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 device infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Dehydration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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
Diabetic ketoacidosis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Electrolyte imbalance			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Failure to thrive			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Hyperglycaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (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
Hyponatraemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	7 / 279 (2.51%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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 2 diabetes mellitus			

subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (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

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

Non-serious adverse events	Global Placebo	Global Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg	China Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	228 / 273 (83.52%)	263 / 278 (94.60%)	24 / 24 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 273 (0.73%)	14 / 278 (5.04%)	0 / 24 (0.00%)
occurrences (all)	2	15	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	36 / 273 (13.19%)	45 / 278 (16.19%)	0 / 24 (0.00%)
occurrences (all)	46	61	0
Chest discomfort			
subjects affected / exposed	2 / 273 (0.73%)	2 / 278 (0.72%)	3 / 24 (12.50%)
occurrences (all)	2	2	4
Fatigue			
subjects affected / exposed	66 / 273 (24.18%)	86 / 278 (30.94%)	7 / 24 (29.17%)
occurrences (all)	73	101	9
Chest pain			
subjects affected / exposed	8 / 273 (2.93%)	9 / 278 (3.24%)	1 / 24 (4.17%)
occurrences (all)	8	15	1
Malaise			
subjects affected / exposed	7 / 273 (2.56%)	9 / 278 (3.24%)	7 / 24 (29.17%)
occurrences (all)	7	11	7
Non-cardiac chest pain			
subjects affected / exposed	17 / 273 (6.23%)	11 / 278 (3.96%)	0 / 24 (0.00%)
occurrences (all)	20	11	0
Oedema peripheral			

subjects affected / exposed	15 / 273 (5.49%)	18 / 278 (6.47%)	1 / 24 (4.17%)
occurrences (all)	19	18	1
Pain			
subjects affected / exposed	3 / 273 (1.10%)	5 / 278 (1.80%)	0 / 24 (0.00%)
occurrences (all)	3	5	0
Pyrexia			
subjects affected / exposed	11 / 273 (4.03%)	43 / 278 (15.47%)	6 / 24 (25.00%)
occurrences (all)	15	54	8
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	55 / 273 (20.15%)	53 / 278 (19.06%)	11 / 24 (45.83%)
occurrences (all)	61	56	14
Dyspnoea			
subjects affected / exposed	40 / 273 (14.65%)	49 / 278 (17.63%)	1 / 24 (4.17%)
occurrences (all)	43	53	1
Haemoptysis			
subjects affected / exposed	8 / 273 (2.93%)	4 / 278 (1.44%)	2 / 24 (8.33%)
occurrences (all)	9	5	2
Productive cough			
subjects affected / exposed	11 / 273 (4.03%)	13 / 278 (4.68%)	6 / 24 (25.00%)
occurrences (all)	11	15	7
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 273 (5.86%)	25 / 278 (8.99%)	2 / 24 (8.33%)
occurrences (all)	17	25	4
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	12 / 273 (4.40%)	43 / 278 (15.47%)	11 / 24 (45.83%)
occurrences (all)	16	50	15
Amylase increased			
subjects affected / exposed	9 / 273 (3.30%)	19 / 278 (6.83%)	2 / 24 (8.33%)
occurrences (all)	12	34	2
Aspartate aminotransferase increased			

subjects affected / exposed	10 / 273 (3.66%)	39 / 278 (14.03%)	10 / 24 (41.67%)
occurrences (all)	10	55	14
Bilirubin conjugated increased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Blood albumin decreased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	4 / 24 (16.67%)
occurrences (all)	0	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 273 (1.83%)	12 / 278 (4.32%)	1 / 24 (4.17%)
occurrences (all)	6	12	1
Blood bilirubin increased			
subjects affected / exposed	3 / 273 (1.10%)	3 / 278 (1.08%)	5 / 24 (20.83%)
occurrences (all)	3	5	5
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	9 / 273 (3.30%)	19 / 278 (6.83%)	3 / 24 (12.50%)
occurrences (all)	10	28	8
Blood sodium decreased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Blood urea increased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	5
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 273 (0.73%)	8 / 278 (2.88%)	2 / 24 (8.33%)
occurrences (all)	3	8	2
Lipase increased			
subjects affected / exposed	11 / 273 (4.03%)	28 / 278 (10.07%)	0 / 24 (0.00%)
occurrences (all)	14	39	0
Neutrophil count decreased			

subjects affected / exposed	15 / 273 (5.49%)	10 / 278 (3.60%)	4 / 24 (16.67%)
occurrences (all)	20	13	4
Platelet count decreased			
subjects affected / exposed	5 / 273 (1.83%)	14 / 278 (5.04%)	1 / 24 (4.17%)
occurrences (all)	11	18	1
Thyroxine free decreased			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	12 / 273 (4.40%)	27 / 278 (9.71%)	6 / 24 (25.00%)
occurrences (all)	12	28	8
White blood cell count decreased			
subjects affected / exposed	7 / 273 (2.56%)	6 / 278 (2.16%)	3 / 24 (12.50%)
occurrences (all)	11	10	4
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences (all)	1	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	24 / 273 (8.79%)	28 / 278 (10.07%)	2 / 24 (8.33%)
occurrences (all)	29	36	2
Headache			
subjects affected / exposed	27 / 273 (9.89%)	49 / 278 (17.63%)	2 / 24 (8.33%)
occurrences (all)	30	57	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 273 (11.36%)	25 / 278 (8.99%)	12 / 24 (50.00%)
occurrences (all)	43	34	15
Leukocytosis			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Leukopenia			
subjects affected / exposed	4 / 273 (1.47%)	2 / 278 (0.72%)	3 / 24 (12.50%)
occurrences (all)	6	2	3
Neutropenia			

subjects affected / exposed	5 / 273 (1.83%)	6 / 278 (2.16%)	0 / 24 (0.00%)
occurrences (all)	8	6	0
Thrombocytopenia			
subjects affected / exposed	7 / 273 (2.56%)	10 / 278 (3.60%)	5 / 24 (20.83%)
occurrences (all)	8	11	7
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 273 (0.73%)	2 / 278 (0.72%)	3 / 24 (12.50%)
occurrences (all)	2	2	3
Abdominal pain upper			
subjects affected / exposed	14 / 273 (5.13%)	11 / 278 (3.96%)	2 / 24 (8.33%)
occurrences (all)	15	12	2
Abdominal pain			
subjects affected / exposed	13 / 273 (4.76%)	22 / 278 (7.91%)	3 / 24 (12.50%)
occurrences (all)	14	24	3
Constipation			
subjects affected / exposed	37 / 273 (13.55%)	51 / 278 (18.35%)	4 / 24 (16.67%)
occurrences (all)	44	60	4
Diarrhoea			
subjects affected / exposed	47 / 273 (17.22%)	88 / 278 (31.65%)	4 / 24 (16.67%)
occurrences (all)	56	126	7
Mouth ulceration			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	2 / 24 (8.33%)
occurrences (all)	0	1	2
Nausea			
subjects affected / exposed	67 / 273 (24.54%)	78 / 278 (28.06%)	4 / 24 (16.67%)
occurrences (all)	75	110	4
Toothache			
subjects affected / exposed	1 / 273 (0.37%)	3 / 278 (1.08%)	2 / 24 (8.33%)
occurrences (all)	1	3	2
Vomiting			
subjects affected / exposed	21 / 273 (7.69%)	47 / 278 (16.91%)	2 / 24 (8.33%)
occurrences (all)	25	60	2
Hepatobiliary disorders			
Hepatic function abnormal			

subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	3 / 24 (12.50%)
occurrences (all)	0	3	3
Liver injury			
subjects affected / exposed	0 / 273 (0.00%)	0 / 278 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	15 / 273 (5.49%)	18 / 278 (6.47%)	0 / 24 (0.00%)
occurrences (all)	15	19	0
Erythema			
subjects affected / exposed	2 / 273 (0.73%)	7 / 278 (2.52%)	2 / 24 (8.33%)
occurrences (all)	2	9	2
Pruritus			
subjects affected / exposed	31 / 273 (11.36%)	80 / 278 (28.78%)	7 / 24 (29.17%)
occurrences (all)	33	100	8
Rash			
subjects affected / exposed	16 / 273 (5.86%)	68 / 278 (24.46%)	4 / 24 (16.67%)
occurrences (all)	16	84	4
Rash maculo-papular			
subjects affected / exposed	9 / 273 (3.30%)	26 / 278 (9.35%)	2 / 24 (8.33%)
occurrences (all)	9	29	6
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	6 / 273 (2.20%)	28 / 278 (10.07%)	2 / 24 (8.33%)
occurrences (all)	7	30	2
Hypothyroidism			
subjects affected / exposed	3 / 273 (1.10%)	30 / 278 (10.79%)	5 / 24 (20.83%)
occurrences (all)	3	34	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 273 (9.52%)	31 / 278 (11.15%)	4 / 24 (16.67%)
occurrences (all)	35	34	5
Back pain			
subjects affected / exposed	22 / 273 (8.06%)	22 / 278 (7.91%)	2 / 24 (8.33%)
occurrences (all)	23	27	2
Muscular weakness			

subjects affected / exposed	7 / 273 (2.56%)	13 / 278 (4.68%)	2 / 24 (8.33%)
occurrences (all)	8	14	2
Myalgia			
subjects affected / exposed	16 / 273 (5.86%)	22 / 278 (7.91%)	1 / 24 (4.17%)
occurrences (all)	18	26	1
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 273 (1.10%)	5 / 278 (1.80%)	0 / 24 (0.00%)
occurrences (all)	3	6	0
Pharyngitis			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	2 / 24 (8.33%)
occurrences (all)	0	2	2
Pneumonia			
subjects affected / exposed	6 / 273 (2.20%)	14 / 278 (5.04%)	3 / 24 (12.50%)
occurrences (all)	7	14	3
Upper respiratory tract infection			
subjects affected / exposed	4 / 273 (1.47%)	14 / 278 (5.04%)	1 / 24 (4.17%)
occurrences (all)	6	16	1
Urinary tract infection			
subjects affected / exposed	8 / 273 (2.93%)	7 / 278 (2.52%)	1 / 24 (4.17%)
occurrences (all)	13	9	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	57 / 273 (20.88%)	101 / 278 (36.33%)	9 / 24 (37.50%)
occurrences (all)	65	125	12
Dehydration			
subjects affected / exposed	7 / 273 (2.56%)	17 / 278 (6.12%)	0 / 24 (0.00%)
occurrences (all)	11	26	0
Hyperglycaemia			
subjects affected / exposed	13 / 273 (4.76%)	19 / 278 (6.83%)	3 / 24 (12.50%)
occurrences (all)	15	23	3
Hypertriglyceridaemia			
subjects affected / exposed	2 / 273 (0.73%)	1 / 278 (0.36%)	2 / 24 (8.33%)
occurrences (all)	4	1	3
Hyperuricaemia			

subjects affected / exposed	1 / 273 (0.37%)	9 / 278 (3.24%)	1 / 24 (4.17%)
occurrences (all)	1	11	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 273 (0.37%)	8 / 278 (2.88%)	3 / 24 (12.50%)
occurrences (all)	1	8	3
Hypokalaemia			
subjects affected / exposed	7 / 273 (2.56%)	20 / 278 (7.19%)	4 / 24 (16.67%)
occurrences (all)	7	30	4
Hypomagnesaemia			
subjects affected / exposed	9 / 273 (3.30%)	15 / 278 (5.40%)	1 / 24 (4.17%)
occurrences (all)	9	21	1
Hyponatraemia			
subjects affected / exposed	15 / 273 (5.49%)	35 / 278 (12.59%)	5 / 24 (20.83%)
occurrences (all)	25	41	9

Non-serious adverse events	China Placebo	China Nivolumab 240 mg	Global Nivolumab 240 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 26 (84.62%)	23 / 25 (92.00%)	244 / 279 (87.46%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	7 / 279 (2.51%)
occurrences (all)	0	0	7
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 26 (7.69%)	3 / 25 (12.00%)	39 / 279 (13.98%)
occurrences (all)	2	3	49
Chest discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences (all)	0	0	2
Fatigue			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	88 / 279 (31.54%)
occurrences (all)	3	0	110
Chest pain			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	10 / 279 (3.58%)
occurrences (all)	2	3	10
Malaise			

subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	6 / 279 (2.15%)
occurrences (all)	1	1	7
Non-cardiac chest pain			
subjects affected / exposed	3 / 26 (11.54%)	0 / 25 (0.00%)	10 / 279 (3.58%)
occurrences (all)	3	0	10
Oedema peripheral			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	16 / 279 (5.73%)
occurrences (all)	0	1	16
Pain			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	7 / 279 (2.51%)
occurrences (all)	1	2	7
Pyrexia			
subjects affected / exposed	4 / 26 (15.38%)	3 / 25 (12.00%)	20 / 279 (7.17%)
occurrences (all)	4	3	23
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 26 (7.69%)	1 / 25 (4.00%)	1 / 279 (0.36%)
occurrences (all)	2	1	1
Cough			
subjects affected / exposed	10 / 26 (38.46%)	6 / 25 (24.00%)	55 / 279 (19.71%)
occurrences (all)	10	7	62
Dyspnoea			
subjects affected / exposed	2 / 26 (7.69%)	1 / 25 (4.00%)	64 / 279 (22.94%)
occurrences (all)	3	1	66
Haemoptysis			
subjects affected / exposed	3 / 26 (11.54%)	2 / 25 (8.00%)	7 / 279 (2.51%)
occurrences (all)	3	2	7
Productive cough			
subjects affected / exposed	5 / 26 (19.23%)	0 / 25 (0.00%)	15 / 279 (5.38%)
occurrences (all)	6	0	18
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	19 / 279 (6.81%)
occurrences (all)	2	0	19
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	4 / 26 (15.38%)	6 / 25 (24.00%)	21 / 279 (7.53%)
occurrences (all)	7	6	23
Amylase increased			
subjects affected / exposed	0 / 26 (0.00%)	3 / 25 (12.00%)	9 / 279 (3.23%)
occurrences (all)	0	3	13
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 26 (11.54%)	7 / 25 (28.00%)	19 / 279 (6.81%)
occurrences (all)	5	7	22
Bilirubin conjugated increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (0.00%)
occurrences (all)	0	2	0
Blood albumin decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	10 / 279 (3.58%)
occurrences (all)	0	2	11
Blood bilirubin increased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	2 / 279 (0.72%)
occurrences (all)	0	2	3
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	0 / 279 (0.00%)
occurrences (all)	1	2	0
Blood creatinine increased			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	11 / 279 (3.94%)
occurrences (all)	1	5	17
Blood sodium decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			

subjects affected / exposed	2 / 26 (7.69%)	3 / 25 (12.00%)	4 / 279 (1.43%)
occurrences (all)	2	3	4
Lipase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	12 / 279 (4.30%)
occurrences (all)	1	0	13
Neutrophil count decreased			
subjects affected / exposed	8 / 26 (30.77%)	4 / 25 (16.00%)	11 / 279 (3.94%)
occurrences (all)	14	6	19
Platelet count decreased			
subjects affected / exposed	3 / 26 (11.54%)	5 / 25 (20.00%)	12 / 279 (4.30%)
occurrences (all)	5	7	18
Thyroxine free decreased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	16 / 279 (5.73%)
occurrences (all)	1	0	17
White blood cell count decreased			
subjects affected / exposed	7 / 26 (26.92%)	2 / 25 (8.00%)	8 / 279 (2.87%)
occurrences (all)	11	2	12
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences (all)	0	0	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	29 / 279 (10.39%)
occurrences (all)	0	0	33
Headache			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	37 / 279 (13.26%)
occurrences (all)	1	1	44
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 26 (38.46%)	4 / 25 (16.00%)	30 / 279 (10.75%)
occurrences (all)	11	6	44
Leukocytosis			

subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	0 / 279 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	3 / 26 (11.54%)	2 / 25 (8.00%)	6 / 279 (2.15%)
occurrences (all)	3	5	10
Neutropenia			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	8 / 279 (2.87%)
occurrences (all)	2	0	9
Thrombocytopenia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	4 / 279 (1.43%)
occurrences (all)	1	0	5
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	2 / 279 (0.72%)
occurrences (all)	1	1	2
Abdominal pain upper			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	10 / 279 (3.58%)
occurrences (all)	0	1	10
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	16 / 279 (5.73%)
occurrences (all)	0	1	18
Constipation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	34 / 279 (12.19%)
occurrences (all)	1	0	35
Diarrhoea			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	59 / 279 (21.15%)
occurrences (all)	2	0	93
Mouth ulceration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 26 (11.54%)	3 / 25 (12.00%)	69 / 279 (24.73%)
occurrences (all)	3	3	84
Toothache			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	2 / 279 (0.72%)
occurrences (all)	0	3	2

Vomiting			
subjects affected / exposed	3 / 26 (11.54%)	0 / 25 (0.00%)	27 / 279 (9.68%)
occurrences (all)	6	0	36
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 26 (3.85%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences (all)	1	0	1
Liver injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	11 / 279 (3.94%)
occurrences (all)	0	0	12
Erythema			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	6 / 279 (2.15%)
occurrences (all)	0	2	9
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	43 / 279 (15.41%)
occurrences (all)	0	2	47
Rash			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	20 / 279 (7.17%)
occurrences (all)	0	2	26
Rash maculo-papular			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	10 / 279 (3.58%)
occurrences (all)	0	0	10
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	18 / 279 (6.45%)
occurrences (all)	0	0	21
Hypothyroidism			
subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	23 / 279 (8.24%)
occurrences (all)	2	6	24
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 26 (3.85%)	2 / 25 (8.00%)	35 / 279 (12.54%)
occurrences (all)	2	3	39
Back pain			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	30 / 279 (10.75%)
occurrences (all)	1	1	36
Muscular weakness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	8 / 279 (2.87%)
occurrences (all)	0	0	8
Myalgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	26 / 279 (9.32%)
occurrences (all)	0	0	31
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 26 (7.69%)	0 / 25 (0.00%)	2 / 279 (0.72%)
occurrences (all)	2	0	2
Pharyngitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	0 / 279 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	15 / 279 (5.38%)
occurrences (all)	0	1	20
Upper respiratory tract infection			
subjects affected / exposed	3 / 26 (11.54%)	0 / 25 (0.00%)	13 / 279 (4.66%)
occurrences (all)	3	0	14
Urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	7 / 279 (2.51%)
occurrences (all)	0	2	7
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 26 (30.77%)	7 / 25 (28.00%)	71 / 279 (25.45%)
occurrences (all)	9	8	76
Dehydration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	10 / 279 (3.58%)
occurrences (all)	0	0	10
Hyperglycaemia			

subjects affected / exposed	1 / 26 (3.85%)	3 / 25 (12.00%)	13 / 279 (4.66%)
occurrences (all)	1	3	20
Hypertriglyceridaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	1 / 279 (0.36%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	2 / 26 (7.69%)	1 / 25 (4.00%)	5 / 279 (1.79%)
occurrences (all)	2	4	5
Hypoalbuminaemia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 25 (8.00%)	5 / 279 (1.79%)
occurrences (all)	0	2	8
Hypokalaemia			
subjects affected / exposed	2 / 26 (7.69%)	2 / 25 (8.00%)	11 / 279 (3.94%)
occurrences (all)	3	4	13
Hypomagnesaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (0.00%)	11 / 279 (3.94%)
occurrences (all)	0	0	14
Hyponatraemia			
subjects affected / exposed	2 / 26 (7.69%)	4 / 25 (16.00%)	22 / 279 (7.89%)
occurrences (all)	3	4	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2017	The protocol was amended to allow enrollment of patients from China.
14 July 2018	BICR-assessed PFS was changed as a primary objective to secondary objective. Tumor mutational burden (TMB) added as a potential predictive biomarker secondary objective.
20 September 2018	Moved OS of nivolumab vs placebo to secondary objectives.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported