Clinical trial results:
An Open-Label, Multicenter Clinical Trial with Nivolumab (BMS-936558) Monotherapy in Subjects with Advanced or Metastatic Squamous Cell (Sq) Non-Small Cell Lung Cancer (NSCLC) who Have Received at Least One Prior Systemic Regimen for the Treatment of Stage IIIb/IV SqNSCLC

Summary

EudraCT number	2014-001285-10
Trial protocol	HU SE DE FI DK PT ES AT GB IE GR RO
Global end of trial date	27 August 2021

Results information

Result version number	v2 (current)
This version publication date	02 November 2022
First version publication date	11 September 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CA209-171

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02409368
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, 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	14 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the incidence of high-grade (CTCAE v4.0 Grades 3-4), treatment-related, select adverse events in subjects with advanced or metastatic SqNSCLC who progressed during or after at least 1 systemic therapy.

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 participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 April 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	Austria: 9
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	Greece: 34
Country: Number of subjects enrolled	Hungary: 51
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Poland: 81
Country: Number of subjects enrolled	Portugal: 28
Country: Number of subjects enrolled	Romania: 79
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	Spain: 232
Country: Number of subjects enrolled	Sweden: 18
Country: Number of subjects enrolled	United Kingdom: 212
Worldwide total number of subjects	812
EEA total number of subjects	561

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)	331
From 65 to 84 years	480
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1 subject was ECOG PS 3 and thus outside the scope of the protocol. There were 2 ECOG classification periods during this study. The first was used in Primary Endpoint analysis. The second was used in Baseline Characteristics, Secondary Endpoint, and AE analysis. 1 subject was lost from initial ECOG Classification but included at Study Completion.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ECOG (PS0)

Arm description:

ECOG Performance Status 0 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

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

Dosage and administration details:

Nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

Arm title	ECOG (PS1)

Arm description:

ECOG Performance Status 1 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

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

Dosage and administration details:

Nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

Arm title	ECOG (PS 2)

Arm description:

ECOG Performance Status 2 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

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

Dosage and administration details:
Nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

Arm title	ECOG (PS3)

Arm description:
ECOG Performance Status 3 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

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

Dosage and administration details:
Nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks

Number of subjects in period 1	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)
Started	172	537	102
Completed	0	0	0
Not completed	172	537	102
Adverse event, serious fatal	1	5	-
Participant withdrew consent	2	3	4
Study drug toxicity	17	42	7
Other Reasons	5	26	2
Maximum clinical benefit	6	5	-
Participant no longer meets study criteria	3	8	3
Adverse event unrelated to study drug	17	49	12
Lost to follow-up	1	5	-
Poor/non-compliance	-	3	2
Disease Progression	113	382	70
Participant request to discontinue study treatment	6	6	2
Administrative reason by sponsor	1	3	-

Number of subjects in period 1	ECOG (PS3)
Started	1
Completed	0
Not completed	1
Adverse event, serious fatal	-
Participant withdrew consent	-
Study drug toxicity	-

Other Reasons	-
Maximum clinical benefit	-
Participant no longer meets study criteria	-
Adverse event unrelated to study drug	-
Lost to follow-up	-
Poor/non-compliance	-
Disease Progression	1
Participant request to discontinue study treatment	-
Administrative reason by sponsor	-

Baseline characteristics

Reporting groups	
Reporting group title	ECOG (PS0)
Reporting group description:	
ECOG Performance Status 0 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS1)
Reporting group description:	
ECOG Performance Status 1 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS 2)
Reporting group description:	
ECOG Performance Status 2 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS3)
Reporting group description:	
ECOG Performance Status 3 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	

Reporting group values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)
Number of subjects	172	537	102
Age categorical Units: Subjects			
Adults (18-64 years)	83	217	31
From 65-84 years	89	320	70
85 years and over	0	0	1
Age Continuous			
"999"=N/A			
Units: years			
arithmetic mean	63.6	66.1	67.9
standard deviation	± 8.28	± 8.27	± 7.29
Sex: Female, Male Units: Participants			
Female	37	111	22
Male	135	426	80
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	3	0
White	165	530	102
More than one race	0	0	0
Unknown or Not Reported	7	2	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13	37	11
Not Hispanic or Latino	159	500	91
Unknown or Not Reported	0	0	0

Reporting group values	ECOG (PS3)	Total	

Number of subjects	1	812	
Age categorical Units: Subjects			
Adults (18-64 years)	0	331	
From 65-84 years	1	480	
85 years and over	0	1	
Age Continuous			
"999"=N/A			
Units: years			
arithmetic mean	71		
standard deviation	± 999	-	
Sex: Female, Male Units: Participants			
Female	1	171	
Male	0	641	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	3	
White	1	798	
More than one race	0	0	
Unknown or Not Reported	0	9	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	61	
Not Hispanic or Latino	1	751	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	ECOG (PS0)
Reporting group description:	
ECOG Performance Status 0 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS1)
Reporting group description:	
ECOG Performance Status 1 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS 2)
Reporting group description:	
ECOG Performance Status 2 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	
Reporting group title	ECOG (PS3)
Reporting group description:	
ECOG Performance Status 3 nivolumab 3 mg/kg as a 60- minute IV infusion every 2 weeks	

Primary: Number of Participants With High Grade (Grade 3, 4 and 5) Treatment Related Select Adverse Events

End point title	Number of Participants With High Grade (Grade 3, 4 and 5) Treatment Related Select Adverse Events[1][2]
End point description:	
The total number of participants with high grade treatment related select adverse events.	
End point type	Primary
End point timeframe:	
From first dose to time of analysis of primary endpoint (approximately up to 34 months)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics were planned for this endpoint

[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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	537	102	
Units: Participants				
Skin	2	7	0	
Gastrointestinal	1	10	0	
Endocrine	4	3	0	
Hepatic	4	12	2	
Pulmonary	2	6	0	
Renal	0	3	1	
Hypersensitivity/ Infusion reaction	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with High Grade Select Adverse Events

End point title	Number of Participants with High Grade Select Adverse

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered study drug and that does not necessarily have a causal relationship with this treatment. Select AEs include Pulmonary toxicity, Gastrointestinal toxicity (diarrhea or colitis, Endocrinopathies, Hepatotoxicity (including asymptomatic LFT elevations), Renal toxicity, Skin toxicity, and Neurological toxicity.

End point type	Secondary

End point timeframe:

From first dose up to 100 days post last dose (up to 76 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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	537	102	
Units: Participants				
Skin	2	7	0	
Gastrointestinal	1	11	0	
Endocrine	5	4	0	
Hepatic	6	19	3	
Pulmonary	3	9	1	
Renal	0	7	1	
Hypersensitivity/ Infusion reaction	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Onset of Any Grade Select Adverse Events

End point title	Median Time to Onset of Any Grade Select Adverse Events[4]

End point description:

Median Time to onset of any grade select adverse events reported up to 100 days after last doseMedian Time to onset of any grade select adverse events reported up to 100 days after last dose. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered study drug and that does not necessarily have a causal relationship with this treatment. Select AEs include Pulmonary toxicity, Gastrointestinal toxicity (diarrhea or colitis, Endocrinopathies, Hepatotoxicity (including asymptomatic LFT elevations), Renal toxicity, Skin toxicity, and Neurological toxicity.

End point type	Secondary

End point timeframe:

From first dose up to 100 days post last dose (up to approximately 65 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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	537	102	
Units: Weeks				
median (full range (min-max))				
Endrocrine	12.79 (4.0 to 121.6)	10.14 (1.9 to 165.1)	19.86 (6.1 to 55.4)	
Gastrointestinal	11.71 (0.1 to 88.0)	8.86 (0.1 to 228.1)	6.00 (0.3 to 64.3)	
Hepatic	26.64 (1.4 to 234.1)	11.43 (2.0 to 90.1)	8.14 (2.0 to 88.1)	
Pulmonary	33.43 (7.4 to 169.4)	11.50 (0.6 to 166.0)	3.93 (0.1 to 26.3)	
Renal	28.86 (4.1 to 129.9)	22.71 (0.1 to 246.0)	10.29 (1.4 to 52.9)	
Skin	12.14 (0.1 to 92.1)	7.86 (0.1 to 200.1)	14.71 (2.1 to 81.7)	
Hypersensitivity/Infusion Reaction	1.93 (1.7 to 2.1)	2.21 (0.3 to 20.3)	2.14 (2.1 to 28.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Resolution of any Grade Select Adverse Events

End point title	Median Time to Resolution of any Grade Select Adverse

End point description:

Median time to resolution of any grade select adverse events reported up to 100 days after last dose. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation subject administered study drug and that does not necessarily have a causal relationship with this treatment. Select AEs include Pulmonary toxicity, Gastrointestinal toxicity (diarrhea or colitis, Endocrinopathies, Hepatotoxicity (including asymptomatic LFT elevations), Renal toxicity, Skin toxicity, and Neurological toxicity. "99999"=N/A

End point type	Secondary

End point timeframe:

From first dose to up to 100 days post last dose (up to approximately 45 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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	537	102	
Units: Weeks				
median (confidence interval 95%)				
Endrocrine	99999 (109.00 to 99999)	169.43 (17.86 to 99999)	99999 (6.14 to 99999)	
Gastrointestinal	2.86 (0.43 to 5.14)	2.00 (1.00 to 3.00)	2.00 (0.43 to 5.71)	
Hepatic	4.57 (2.57 to 6.14)	7.71 (4.86 to 17.14)	3.57 (2.14 to 8.14)	

Pulmonary	3.00 (1.43 to 99999)	4.29 (2.14 to 6.00)	2.29 (1.00 to 99999)	
Renal	10.14 (2.14 to 99999)	6.14 (2.29 to 25.14)	59.14 (0.57 to 59.14)	
Skin	99999 (13.57 to 99999)	15.43 (8.71 to 52.86)	5.71 (2.00 to 99999)	
Hypersensitivity/Infusion Reaction	1.14 (0.14 to 2.14)	0.14 (0.14 to 4.43)	0.14 (0.14 to 0.71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival[6]

End point description:

Overall Survival (OS) is defined as the time from first dosing date to the date of death. A subject who has not died will be censored at last known date alive. OS will be followed continuously while subjects are on treatment and every 3 months via in-person or phone contact after subjects discontinue the study drug.

End point type	Secondary

End point timeframe:

From the first dosing up to the date of death (up to approximately 76 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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	537	102	
Units: Months				
median (confidence interval 95%)	12.1 (9.9 to 13.4)	10.3 (9.3 to 11.3)	5.2 (3.0 to 7.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[7]

End point description:

ORR is defined as the percentage of subjects with a best overall response (BOR) of confirmed CR or PR with respect to all treated participants. ORR as assessed by the investigator will be reported.

End point type	Secondary

End point timeframe:

From first dose up to last dose (up to approximately 76 months)

Notes:

[7] - 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: Only summary statistics were planned for this endpoint

End point values	ECOG (PS0)	ECOG (PS1)	ECOG (PS 2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	456	64	
Units: Percentage				
number (confidence interval 95%)	8.0 (4.2 to 13.6)	11.0 (8.2 to 14.2)	1.6 (0.0 to 8.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs/SAEs are reported from start of the treatment until the end of treatment + 100 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	ECOG Performance Status 0
Reporting group description: Nivolumab 3 mg/kg as a 60-minute IV infusion every 2 weeks	
Reporting group title	ECOG Performance Status 2
Reporting group description: Nivolumab 3 mg/kg as a 60-minute IV infusion every 2 weeks	
Reporting group title	ECOG Performance Status 3
Reporting group description: Nivolumab 3 mg/kg as a 60-minute IV infusion every 2 weeks	
Reporting group title	ECOG Performance Status 1
Reporting group description: Nivolumab 3 mg/kg as a 60-minute IV infusion every 2 weeks	

Serious adverse events	ECOG Performance Status 0	ECOG Performance Status 2	ECOG Performance Status 3
Total subjects affected by serious adverse events			
subjects affected / exposed	115 / 172 (66.86%)	84 / 102 (82.35%)	1 / 1 (100.00%)
number of deaths (all causes)	131	90	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 neoplasm			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain cancer metastatic			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	3 / 172 (1.74%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Follicular thyroid cancer			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Malignant neoplasm progression			
subjects affected / exposed	59 / 172 (34.30%)	58 / 102 (56.86%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 60	0 / 59	0 / 0
deaths causally related to treatment / all	0 / 57	0 / 56	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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-small cell lung cancer metastatic			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Oncologic complication			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 intestine adenocarcinoma			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 172 (0.58%)	2 / 102 (1.96%)	0 / 1 (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
Tumour compression			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour associated fever			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Embolism			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 ischaemia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Superior vena cava occlusion			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Fatigue			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Hernia obstructive			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Pain			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Oedema peripheral			

subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Pyrexia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Sudden death			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Aspiration			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 172 (0.00%)	2 / 102 (1.96%)	0 / 1 (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

Asthma			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Atelectasis			
subjects affected / exposed	2 / 172 (1.16%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumopathy			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	9 / 172 (5.23%)	10 / 102 (9.80%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	1 / 10	0 / 11	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Epistaxis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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	7 / 172 (4.07%)	3 / 102 (2.94%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 4	0 / 0
deaths causally related to treatment / all	1 / 3	0 / 2	0 / 0
Hypoxia			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 consolidation			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Oesophagobronchial fistula			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Pleural effusion			
subjects affected / exposed	3 / 172 (1.74%)	2 / 102 (1.96%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	4 / 172 (2.33%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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 embolism			
subjects affected / exposed	3 / 172 (1.74%)	0 / 102 (0.00%)	0 / 1 (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
Pulmonary haemorrhage			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Respiratory tract haemorrhage			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Respiratory failure			
subjects affected / exposed	3 / 172 (1.74%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Tracheal stenosis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Liver function test increased			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Accidental overdose			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	2 / 102 (1.96%)	0 / 1 (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
Femur fracture			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Infusion related reaction			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 172 (0.00%)	2 / 102 (1.96%)	0 / 1 (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
Radiation oesophagitis			

subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Skull fractured base			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Subdural haematoma			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 limb fracture			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Atrial fibrillation			
subjects affected / exposed	2 / 172 (1.16%)	2 / 102 (1.96%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 arrest			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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 congestive			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Cardiomegaly			

subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve prolapse			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	2 / 172 (1.16%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pericarditis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Sinus tachycardia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular extrasystoles			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Cerebral haemorrhage			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Coma			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Dizziness			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Epilepsy			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Intracranial pressure increased			

subjects affected / exposed	2 / 172 (1.16%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Motor dysfunction			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Seizure			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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 cord compression			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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 / 172 (0.00%)	3 / 102 (2.94%)	0 / 1 (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
Tremor			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	2 / 172 (1.16%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 fissure			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Autoimmune colitis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 microscopic			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Dysphagia			

subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Gastric ulcer			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 disorder			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Inguinal hernia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal rupture			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Oesophageal stenosis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Vomiting			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	2 / 102 (1.96%)	0 / 1 (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
Biliary tract disorder			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Hepatic failure			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 hepatitis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Liver injury			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 macular			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Calculus urinary			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocyturia			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Nephrolithiasis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			

subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	2 / 172 (1.16%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Hypophysitis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Thyroiditis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	2 / 172 (1.16%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Pain in extremity			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patellofemoral pain syndrome			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Abscess			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Bacteraemia			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Bacterial diarrhoea			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 infection			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Biliary sepsis			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	4 / 172 (2.33%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 colitis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 172 (0.00%)	2 / 102 (1.96%)	0 / 1 (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
H1N1 influenza			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	5 / 172 (2.91%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinitis			
subjects affected / exposed	0 / 172 (0.00%)	1 / 102 (0.98%)	0 / 1 (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
Meningitis aseptic			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	20 / 172 (11.63%)	10 / 102 (9.80%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 22	0 / 11	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 fungal			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 pneumococcal			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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 tuberculosis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	11 / 172 (6.40%)	3 / 102 (2.94%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 14	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	3 / 172 (1.74%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Staphylococcal infection			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Urinary tract infection			
subjects affected / exposed	1 / 172 (0.58%)	1 / 102 (0.98%)	0 / 1 (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
Vulval abscess			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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			
Decreased appetite			

subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Dehydration			
subjects affected / exposed	2 / 172 (1.16%)	1 / 102 (0.98%)	0 / 1 (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
Diabetes mellitus			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 172 (0.58%)	3 / 102 (2.94%)	0 / 1 (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
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			

subjects affected / exposed	1 / 172 (0.58%)	0 / 102 (0.00%)	0 / 1 (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
Hypoglycaemia			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
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 / 172 (0.00%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 172 (1.16%)	2 / 102 (1.96%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ECOG Performance Status 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	375 / 537 (69.83%)		
number of deaths (all causes)	446		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder neoplasm			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Brain cancer metastatic				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cancer pain				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Follicular thyroid cancer				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm progression				
subjects affected / exposed	206 / 537 (38.36%)			
occurrences causally related to treatment / all	0 / 210			
deaths causally related to treatment / all	0 / 198			
Lung neoplasm malignant				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metastases to central nervous system				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metastases to lymph nodes				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer metastatic				

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oncologic complication				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Small intestine adenocarcinoma				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	5 / 537 (0.93%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Tumour compression				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour associated fever				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Superior vena cava occlusion				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chest pain				

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Fatigue				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Hernia obstructive				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				

subjects affected / exposed	8 / 537 (1.49%)			
occurrences causally related to treatment / all	1 / 8			
deaths causally related to treatment / all	0 / 0			
Sudden cardiac death				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sudden death				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	1 / 4			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Drug hypersensitivity				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Aspiration				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute respiratory failure				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Atelectasis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	7 / 537 (1.30%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Bronchopneumopathy				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	28 / 537 (5.21%)			
occurrences causally related to treatment / all	4 / 31			
deaths causally related to treatment / all	0 / 1			
Epistaxis				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	11 / 537 (2.05%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 3			
Hypoxia				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immune-mediated lung disease				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung consolidation				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagobronchial fistula				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	10 / 537 (1.86%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	15 / 537 (2.79%)			
occurrences causally related to treatment / all	14 / 16			
deaths causally related to treatment / all	2 / 2			
Pneumothorax				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pulmonary embolism				

subjects affected / exposed	6 / 537 (1.12%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
Pulmonary haemorrhage				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Respiratory tract haemorrhage				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	10 / 537 (1.86%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 3			
Tracheal stenosis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Agitation				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Mania				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accidental overdose				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foreign body in gastrointestinal tract				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation oesophagitis				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fractured base				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Rib fracture				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Splenic rupture				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tracheal obstruction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Tracheo-oesophageal fistula				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				

Atrial fibrillation			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Atrial flutter			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	3 / 537 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	3 / 537 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Cardiomegaly			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mitral valve prolapse				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Myocardial infarction				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Sinus tachycardia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular extrasystoles				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Brain oedema				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Coma				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lacunar infarction				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Monoparesis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Motor dysfunction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				

subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 537 (1.12%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anal fissure			

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autoimmune colitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Colitis microscopic				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	7 / 537 (1.30%)			
occurrences causally related to treatment / all	4 / 7			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorder				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune-mediated enterocolitis				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal rupture				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Autoimmune hepatitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Biliary tract disorder				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune-mediated hepatitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Jaundice cholestatic				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver injury				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin and subcutaneous tissue disorders				
Angioedema				

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rash macular				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukocyturia				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	4 / 537 (0.74%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract obstruction				

subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophysitis			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroiditis			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Arthritis			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 537 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	0 / 537 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Patellofemoral pain syndrome			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			

subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial diarrhoea				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary sepsis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis				

subjects affected / exposed	9 / 537 (1.68%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Bronchitis bacterial				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Clostridium colitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				

subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	21 / 537 (3.91%)			
occurrences causally related to treatment / all	2 / 25			
deaths causally related to treatment / all	0 / 1			
Mediastinitis				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis aseptic				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Parainfluenzae virus infection				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	41 / 537 (7.64%)		
occurrences causally related to treatment / all	2 / 47		
deaths causally related to treatment / all	0 / 10		
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia fungal			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia pneumococcal			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	3 / 537 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary tuberculosis			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	25 / 537 (4.66%)		
occurrences causally related to treatment / all	0 / 26		
deaths causally related to treatment / all	0 / 2		
Sepsis			
subjects affected / exposed	7 / 537 (1.30%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Septic shock			

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal infection				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	3 / 537 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection				
subjects affected / exposed	5 / 537 (0.93%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Vulval abscess				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cachexia				

subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	12 / 537 (2.23%)			
occurrences causally related to treatment / all	2 / 14			
deaths causally related to treatment / all	0 / 0			
Diabetic metabolic decompensation				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoalbuminaemia				
subjects affected / exposed	1 / 537 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				

subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	3 / 537 (0.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ECOG Performance Status 0	ECOG Performance Status 2	ECOG Performance Status 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	149 / 172 (86.63%)	86 / 102 (84.31%)	1 / 1 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 172 (6.98%)	0 / 102 (0.00%)	0 / 1 (0.00%)
occurrences (all)	15	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	30 / 172 (17.44%)	15 / 102 (14.71%)	0 / 1 (0.00%)
occurrences (all)	46	19	0
Fatigue			
subjects affected / exposed	40 / 172 (23.26%)	25 / 102 (24.51%)	1 / 1 (100.00%)
occurrences (all)	48	32	1
Chest pain			
subjects affected / exposed	10 / 172 (5.81%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences (all)	11	1	0
Non-cardiac chest pain			
subjects affected / exposed	6 / 172 (3.49%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	6	8	0
Oedema peripheral			

subjects affected / exposed	7 / 172 (4.07%)	14 / 102 (13.73%)	1 / 1 (100.00%)
occurrences (all)	8	16	1
Pyrexia			
subjects affected / exposed	9 / 172 (5.23%)	8 / 102 (7.84%)	0 / 1 (0.00%)
occurrences (all)	11	10	0
Influenza like illness			
subjects affected / exposed	3 / 172 (1.74%)	2 / 102 (1.96%)	1 / 1 (100.00%)
occurrences (all)	4	2	3
Peripheral swelling			
subjects affected / exposed	2 / 172 (1.16%)	2 / 102 (1.96%)	1 / 1 (100.00%)
occurrences (all)	2	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	44 / 172 (25.58%)	19 / 102 (18.63%)	0 / 1 (0.00%)
occurrences (all)	54	23	0
Dyspnoea			
subjects affected / exposed	44 / 172 (25.58%)	28 / 102 (27.45%)	1 / 1 (100.00%)
occurrences (all)	61	31	1
Haemoptysis			
subjects affected / exposed	11 / 172 (6.40%)	10 / 102 (9.80%)	0 / 1 (0.00%)
occurrences (all)	12	12	0
Pneumonitis			
subjects affected / exposed	10 / 172 (5.81%)	2 / 102 (1.96%)	0 / 1 (0.00%)
occurrences (all)	11	2	0
Productive cough			
subjects affected / exposed	3 / 172 (1.74%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	3	7	0
Pleural effusion			
subjects affected / exposed	2 / 172 (1.16%)	1 / 102 (0.98%)	1 / 1 (100.00%)
occurrences (all)	2	1	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 172 (5.23%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences (all)	9	1	0
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	15 / 172 (8.72%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	23	5	0
Alanine aminotransferase increased			
subjects affected / exposed	12 / 172 (6.98%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	20	5	0
Blood creatinine increased			
subjects affected / exposed	9 / 172 (5.23%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	13	5	0
Weight decreased			
subjects affected / exposed	8 / 172 (4.65%)	7 / 102 (6.86%)	0 / 1 (0.00%)
occurrences (all)	8	7	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 172 (1.74%)	8 / 102 (7.84%)	0 / 1 (0.00%)
occurrences (all)	3	8	0
Headache			
subjects affected / exposed	10 / 172 (5.81%)	3 / 102 (2.94%)	0 / 1 (0.00%)
occurrences (all)	16	3	0
Seizure			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	23 / 172 (13.37%)	21 / 102 (20.59%)	1 / 1 (100.00%)
occurrences (all)	25	35	1
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 172 (1.16%)	3 / 102 (2.94%)	0 / 1 (0.00%)
occurrences (all)	2	4	0
Constipation			

subjects affected / exposed	18 / 172 (10.47%)	16 / 102 (15.69%)	0 / 1 (0.00%)
occurrences (all)	18	18	0
Diarrhoea			
subjects affected / exposed	26 / 172 (15.12%)	16 / 102 (15.69%)	0 / 1 (0.00%)
occurrences (all)	46	27	0
Nausea			
subjects affected / exposed	20 / 172 (11.63%)	16 / 102 (15.69%)	0 / 1 (0.00%)
occurrences (all)	27	20	0
Stomatitis			
subjects affected / exposed	5 / 172 (2.91%)	7 / 102 (6.86%)	0 / 1 (0.00%)
occurrences (all)	9	7	0
Vomiting			
subjects affected / exposed	9 / 172 (5.23%)	9 / 102 (8.82%)	1 / 1 (100.00%)
occurrences (all)	11	15	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	7 / 172 (4.07%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	8	6	0
Pruritus			
subjects affected / exposed	9 / 172 (5.23%)	10 / 102 (9.80%)	0 / 1 (0.00%)
occurrences (all)	9	12	0
Rash			
subjects affected / exposed	10 / 172 (5.81%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	12	5	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	13 / 172 (7.56%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences (all)	15	1	0
Hypothyroidism			
subjects affected / exposed	25 / 172 (14.53%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	25	6	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	11 / 172 (6.40%)	7 / 102 (6.86%)	1 / 1 (100.00%)
occurrences (all)	15	8	1
Arthralgia			

subjects affected / exposed	24 / 172 (13.95%)	7 / 102 (6.86%)	1 / 1 (100.00%)
occurrences (all)	27	7	1
Pain in extremity			
subjects affected / exposed	4 / 172 (2.33%)	6 / 102 (5.88%)	1 / 1 (100.00%)
occurrences (all)	4	6	1
Musculoskeletal chest pain			
subjects affected / exposed	7 / 172 (4.07%)	7 / 102 (6.86%)	0 / 1 (0.00%)
occurrences (all)	7	8	0
Groin pain			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	18 / 172 (10.47%)	7 / 102 (6.86%)	0 / 1 (0.00%)
occurrences (all)	23	12	0
Nasopharyngitis			
subjects affected / exposed	11 / 172 (6.40%)	1 / 102 (0.98%)	0 / 1 (0.00%)
occurrences (all)	15	1	0
Pneumonia			
subjects affected / exposed	11 / 172 (6.40%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	12	6	0
Respiratory tract infection			
subjects affected / exposed	10 / 172 (5.81%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	14	7	0
Upper respiratory tract infection			
subjects affected / exposed	10 / 172 (5.81%)	2 / 102 (1.96%)	0 / 1 (0.00%)
occurrences (all)	15	2	0
Catheter site infection			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	4 / 172 (2.33%)	3 / 102 (2.94%)	1 / 1 (100.00%)
occurrences (all)	5	5	1
Tooth infection			
subjects affected / exposed	2 / 172 (1.16%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	3	0	1

Oral fungal infection			
subjects affected / exposed	0 / 172 (0.00%)	0 / 102 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 172 (13.95%)	24 / 102 (23.53%)	0 / 1 (0.00%)
occurrences (all)	31	32	0
Hypercalcaemia			
subjects affected / exposed	6 / 172 (3.49%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	12	6	0
Hyperkalaemia			
subjects affected / exposed	7 / 172 (4.07%)	6 / 102 (5.88%)	0 / 1 (0.00%)
occurrences (all)	12	7	0
Hypomagnesaemia			
subjects affected / exposed	11 / 172 (6.40%)	5 / 102 (4.90%)	0 / 1 (0.00%)
occurrences (all)	28	6	0

Non-serious adverse events	ECOG Performance Status 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	472 / 537 (87.90%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 537 (3.54%)		
occurrences (all)	31		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	131 / 537 (24.39%)		
occurrences (all)	170		
Fatigue			
subjects affected / exposed	121 / 537 (22.53%)		
occurrences (all)	160		
Chest pain			
subjects affected / exposed	24 / 537 (4.47%)		
occurrences (all)	25		
Non-cardiac chest pain			

subjects affected / exposed	34 / 537 (6.33%)		
occurrences (all)	37		
Oedema peripheral			
subjects affected / exposed	30 / 537 (5.59%)		
occurrences (all)	32		
Pyrexia			
subjects affected / exposed	49 / 537 (9.12%)		
occurrences (all)	59		
Influenza like illness			
subjects affected / exposed	4 / 537 (0.74%)		
occurrences (all)	5		
Peripheral swelling			
subjects affected / exposed	8 / 537 (1.49%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	134 / 537 (24.95%)		
occurrences (all)	160		
Dyspnoea			
subjects affected / exposed	167 / 537 (31.10%)		
occurrences (all)	204		
Haemoptysis			
subjects affected / exposed	47 / 537 (8.75%)		
occurrences (all)	59		
Pneumonitis			
subjects affected / exposed	22 / 537 (4.10%)		
occurrences (all)	26		
Productive cough			
subjects affected / exposed	26 / 537 (4.84%)		
occurrences (all)	30		
Pleural effusion			
subjects affected / exposed	6 / 537 (1.12%)		
occurrences (all)	6		
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	12 / 537 (2.23%) 13		
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	 28 / 537 (5.21%) 40 30 / 537 (5.59%) 41 34 / 537 (6.33%) 55 42 / 537 (7.82%) 45		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Seizure subjects affected / exposed occurrences (all)	 28 / 537 (5.21%) 33 36 / 537 (6.70%) 42 2 / 537 (0.37%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 97 / 537 (18.06%) 126		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	 1 / 537 (0.19%) 1		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	28 / 537 (5.21%) 34		
Constipation subjects affected / exposed occurrences (all)	80 / 537 (14.90%) 88		
Diarrhoea subjects affected / exposed occurrences (all)	100 / 537 (18.62%) 164		
Nausea subjects affected / exposed occurrences (all)	71 / 537 (13.22%) 85		
Stomatitis subjects affected / exposed occurrences (all)	14 / 537 (2.61%) 19		
Vomiting subjects affected / exposed occurrences (all)	34 / 537 (6.33%) 45		
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	26 / 537 (4.84%) 27		
Pruritus subjects affected / exposed occurrences (all)	58 / 537 (10.80%) 76		
Rash subjects affected / exposed occurrences (all)	39 / 537 (7.26%) 41		
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	18 / 537 (3.35%) 19		
Hypothyroidism subjects affected / exposed occurrences (all)	37 / 537 (6.89%) 40		
Musculoskeletal and connective tissue disorders			

Back pain				
subjects affected / exposed	46 / 537 (8.57%)			
occurrences (all)	56			
Arthralgia				
subjects affected / exposed	52 / 537 (9.68%)			
occurrences (all)	63			
Pain in extremity				
subjects affected / exposed	25 / 537 (4.66%)			
occurrences (all)	28			
Musculoskeletal chest pain				
subjects affected / exposed	24 / 537 (4.47%)			
occurrences (all)	26			
Groin pain				
subjects affected / exposed	2 / 537 (0.37%)			
occurrences (all)	2			
Infections and infestations				
Lower respiratory tract infection				
subjects affected / exposed	51 / 537 (9.50%)			
occurrences (all)	73			
Nasopharyngitis				
subjects affected / exposed	15 / 537 (2.79%)			
occurrences (all)	21			
Pneumonia				
subjects affected / exposed	24 / 537 (4.47%)			
occurrences (all)	31			
Respiratory tract infection				
subjects affected / exposed	37 / 537 (6.89%)			
occurrences (all)	45			
Upper respiratory tract infection				
subjects affected / exposed	29 / 537 (5.40%)			
occurrences (all)	38			
Catheter site infection				
subjects affected / exposed	0 / 537 (0.00%)			
occurrences (all)	0			
Oral candidiasis				

subjects affected / exposed	26 / 537 (4.84%)		
occurrences (all)	33		
Tooth infection			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences (all)	1		
Oral fungal infection			
subjects affected / exposed	1 / 537 (0.19%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	147 / 537 (27.37%)		
occurrences (all)	173		
Hypercalcaemia			
subjects affected / exposed	39 / 537 (7.26%)		
occurrences (all)	50		
Hyperkalaemia			
subjects affected / exposed	20 / 537 (3.72%)		
occurrences (all)	27		
Hypomagnesaemia			
subjects affected / exposed	27 / 537 (5.03%)		
occurrences (all)	43		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2014	The inclusion criteria have been expanded and the exclusion criteria have been minimized in order to expand the subject population. The background section has also been updated to reflect the most recently available data. Expanded palliative local therapy. Randomization after 1 year to subjects who are still benefitting from treatment and achieved a partial or complete response to offer insight into the optimal treatment duration of nivolumab has been added. After 1 year of therapy, subjects will be randomized to continue nivolumab monotherapy (Cohort A) or discontinue therapy with the option of retreatment disease progression (Cohort B). The requirement to have a separate assessment plan for the subjects in the Performance Status 2 (PS2) subgroup has been eliminated. The EQ-5D has been removed. Lung Cancer Symptom Survey has also been eliminated from the subject follow up and decreased while on treatment. Initial tumor assessments have also been changed to occur at Week 8 instead of Week 6. The statistical section has been reformatted. The phrase "rate and frequency" has been changed to the term "incidence" throughout the protocol. The term "Adverse Events of Special Interest" has been changed to "Select Adverse Events." The Performance Status groups were renamed "Subgroup" (from "Cohort") to avoid confusion with the randomized cohorts. Treatment discontinuation criteria were moved from Section 3.5 to the newly created Section 4.6.5.1 to follow the nivolumab protocol structure. The requirement for electrocardiograms has been removed as these tests are not done within the nivolumab clinical development program any more.
18 June 2015	The sample size was reduced from 1800 to 950 (with 15% screening failure rate, 800 will be treated); second-line lung cancer patients will now be allowed to enroll in the study; and the randomization at one year into Cohort A and Cohort B has been removed.
26 October 2016	Adjustment to PS 0-1 and PS 2 subgroup sample numbers. Changes to informed consent procedure for treatment beyond disease progression. Clarification of SAE reporting to within 100 days of discontinuation of drug. Clarification of LCSS and TFT assessments timepoints. Addition of CBC/ TFTs to off-treatment follow-up scheduled lab test. Addition that dose must be recalculated if weight on the day of dosing differs by > 10% from the weight used to calculate the dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported