



Clinical trial results:

A Phase IIIb/IV Safety Trial of Flat Dose Nivolumab in Combination with Ipilimumab in Participants with Non-Small Cell Lung Cancer CheckMate 817, CHECKpoint pathway and nivoluMAB clinical Trial Evaluation

Summary

EudraCT number	2016-002621-10
Trial protocol	FR ES HU GB BE CZ PL IT GR DE RO NL
Global end of trial date	13 May 2022

Results information

Result version number	v1 (current)
This version publication date	
First version publication date	

Trial information

Trial identification

Sponsor protocol code	CA209-817
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 International Corporation, EU Study Start-Up Unit, 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	29 July 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the safety of Nivolumab flat dosing in combination with weight-based Ipilimumab administration in participants with Non-Small Cell Lung Cancer (NSCLC)

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	05 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 21
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Canada: 54
Country: Number of subjects enrolled	Chile: 28
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	United States: 229
Country: Number of subjects enrolled	Belgium: 37
Country: Number of subjects enrolled	Czechia: 11
Country: Number of subjects enrolled	France: 92
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Greece: 23
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	Italy: 76
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Poland: 53
Country: Number of subjects enrolled	Romania: 75
Country: Number of subjects enrolled	Spain: 146
Country: Number of subjects enrolled	United Kingdom: 45
Country: Number of subjects enrolled	Switzerland: 23
Country: Number of subjects enrolled	Russian Federation: 25

Country: Number of subjects enrolled	Turkey: 6
Worldwide total number of subjects	1041
EEA total number of subjects	595

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)	488
From 65 to 84 years	546
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Analysis for the NSCLC special population cohort A1 is pre-specified as exploratory.

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	Cohort A

Arm description:

First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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

Dosage and administration details:

1 mg/kg Q6W

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

Dosage and administration details:

240 mg Q2W

Arm title	Cohort A1
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Arm description:

First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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

Dosage and administration details:

1 mg/kg Q6W

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg Q2W

Arm title	Cohort B
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Arm description:

Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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

Dosage and administration details:

1 mg/kg Q6W

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

Dosage and administration details:

240 mg Q2W

Arm title	Cohort C
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Arm description:

First-line NSCLC high tumor mutational burden (H-TMB \geq 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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

Dosage and administration details:

1 mg/kg Q6W

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

Dosage and administration details:

240 mg Q2W

Number of subjects in period 1	Cohort A	Cohort A1	Cohort B
Started	391	198	395
Completed	56	16	30
Not completed	335	182	365
Adverse event, serious fatal	7	3	5
Consent withdrawn by subject	5	2	7
Disease progression	184	109	260
Adverse Event unrelated to study drug	30	18	21
Study drug toxicity	90	32	55
Maximum clinical benefit	5	2	1
Participant no longer meets study criteria	-	1	1
Other reasons	4	8	6
Poor/Non-compliance	-	2	1
Lost to follow-up	-	-	2
Participant request to discontinue study treatment	10	5	5
Administrative reason by sponsor	-	-	1

Number of subjects in period 1	Cohort C
Started	57
Completed	12
Not completed	45
Adverse event, serious fatal	1
Consent withdrawn by subject	2
Disease progression	19
Adverse Event unrelated to study drug	6
Study drug toxicity	14
Maximum clinical benefit	-
Participant no longer meets study criteria	-
Other reasons	-
Poor/Non-compliance	-
Lost to follow-up	-
Participant request to discontinue study treatment	3
Administrative reason by sponsor	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort A
Reporting group description: First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort A1
Reporting group description: First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort B
Reporting group description: Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort C
Reporting group description: First-line NSCLC high tumor mutational burden (H-TMB \geq 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	

Reporting group values	Cohort A	Cohort A1	Cohort B
Number of subjects	391	198	395
Age Categorical Units: Participants			
< 65 years old	183	81	200
\geq 65 and < 85 years old	206	115	195
\geq 85 years old	2	2	0
Sex: Female, Male Units: Participants			
Female	155	71	128
Male	236	127	267
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	0	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	3	5
White	379	194	382
More than one race	0	0	0
Unknown or Not Reported	3	1	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	10	13	12
Not Hispanic or Latino	185	78	175
Unknown or Not Reported	196	107	208

Reporting group values	Cohort C	Total	
Number of subjects	57	1041	
Age Categorical Units: Participants			
< 65 years old	24	488	
>= 65 and < 85 years old	30	546	
>= 85 years old	3	7	
Sex: Female, Male Units: Participants			
Female	29	383	
Male	28	658	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	7	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	8	22	
White	47	1002	
More than one race	0	0	
Unknown or Not Reported	2	10	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	38	
Not Hispanic or Latino	54	492	
Unknown or Not Reported	0	511	

End points

End points reporting groups

Reporting group title	Cohort A
Reporting group description: First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort A1
Reporting group description: First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort B
Reporting group description: Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	
Reporting group title	Cohort C
Reporting group description: First-line NSCLC high tumor mutational burden (H-TMB \geq 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first	

Primary: Number of Participants with High Grade (Grade 3-4 and Grade 5) Drug-Related Select Adverse Events (AEs)

End point title	Number of Participants with High Grade (Grade 3-4 and Grade 5) Drug-Related Select Adverse Events (AEs) ^{[1][2]}
End point description: Drug related AEs are those events with relationship to study drug. If the relationship to study drug is missing, the AE will be considered as drug-related. The select AEs of interest are the following: Pulmonary, Renal, Gastrointestinal, Hepatic, Skin, Endocrine, and hypersensitivity/infusion reaction events. AEs are reported using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4. Grade 3= Prolonged severe reaction Grade 4= Life threatening Grade 5= Death	
End point type	Primary
End point timeframe: From first dose to 30 days post last dose (Up to approximately 27 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 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 pre-specified arms planned for this endpoint.	

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	395	57	
Units: Participants				
Gastrointestinal AEs grade 3-4	19	15	4	
Gastrointestinal AEs grade 5	0	0	0	
Hepatic AEs grade 3-4	25	17	3	
Hepatic AEs grade 5	0	0	0	
Pulmonary AEs grade 3-4	18	11	2	
Pulmonary AEs grade 5	0	1	0	
Renal AEs grade 3-4	2	1	1	
Renal AEs grade 5	0	0	0	
Skin AEs grade 3-4	14	9	2	
Skin AEs grade 5	0	0	0	
Endocrine AEs grade 3-4	18	11	2	
Endocrine AEs grade 5	0	0	0	
Hypersensitivity/Infusion Reaction grade 3-4	6	3	0	
Hypersensitivity/Infusion Reaction grade 5	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with High Grade (Grade 3-4 and Grade 5) Immune-Mediated Adverse Events (imAEs)

End point title	Number of Participants with High Grade (Grade 3-4 and Grade 5) Immune-Mediated Adverse Events (imAEs) ^{[3][4]}
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End point description:

imAEs are specific events that include pneumonitis, diarrhea/colitis, hepatitis, nephritis/renal dysfunction, rash, and endocrine (adrenal insufficiency, hypothyroidism/thyroiditis, hyperthyroidism, diabetes mellitus, and hypophysitis). AEs are reported using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.

Grade 3= Prolonged severe reaction

Grade 4= Life threatening

Grade 5= Death

End point type	Primary
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End point timeframe:

From first dose to 100 days post last dose (Up to approximately 29 months)

Notes:

[3] - 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 planned for this endpoint.

[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 pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	395	57	
Units: Participants				
Pneumonitis grade 3-4	20	14	3	
Diarrhea/Colitis grade 3-4	19	15	3	
Hepatitis grade 3-4	18	13	1	
Adrenal Insufficiency grade 3-4	5	4	1	
Hypothyroidism/Thyroiditis grade 3-4	2	2	0	
Hypothyroidism grade 3-4	1	1	0	
Thyroiditis grade 3-4	1	1	0	
Diabetes Mellitus grade 3-4	1	0	0	
Nephritis and Renal Dysfunction grade 3-4	2	1	0	
Rash grade 3-4	14	8	1	
Hypersensitivity grade 3-4	4	2	0	
Hyperthyroidism grade 3-4	0	2	0	
Hypophysitis grade 3-4	3	1	1	
Any category imAEs grade 5	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS) ^[5]
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End point description:

PFS is defined as the time from first dosing date to the date of the first documented tumor progression, as determined by investigators (per RECIST v1.1), or death due to any cause, whichever occurs first. Progressive Disease (PD)= $\geq 20\%$ increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of ≥ 5 mm. The appearance of one or more new lesions is also considered progression.

End point type	Secondary
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End point timeframe:

From first dosing date to the date of first documented tumor progression or, death due to any cause, whichever occurs first (Up to approximately 67 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 pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	395	57	
Units: Months				
median (confidence interval 95%)	5.75 (4.50 to 7.62)	3.91 (2.89 to 4.24)	11.10 (6.47 to 18.40)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title | Duration of Response (DoR)^[6]

End point description:

DoR is defined as the time between the date of first confirmed complete response (CR) or partial response (PR) to the date of the first documented tumor progression per RECIST 1.1, or death due to any cause, whichever occurs first.

CR= Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.

PR= $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Progressive Disease (PD)= $\geq 20\%$ increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of ≥ 5 mm.

The appearance of one or more new lesions is also considered progression.

99999=Not available

End point type | Secondary

End point timeframe:

From first dosing date to the date of first documented tumor progression or, death due to any cause, whichever occurs first (Up to approximately 67 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 pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	90	26	
Units: Months				
median (confidence interval 95%)	27.56 (20.40 to 36.04)	13.01 (10.12 to 19.29)	26.05 (12.22 to 99999)	

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 participants with a best overall response of confirmed complete response (CR) or partial response (PR).

CR= Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.

PR= $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

End point type | Secondary

End point timeframe:

From first dosing date up to approximately 67 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 pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	395	57	
Units: Percentage of participants				
number (confidence interval 95%)	37.3 (32.5 to 42.3)	22.8 (18.7 to 27.2)	45.6 (32.4 to 59.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS) ^[8]
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End point description:

OS is defined as the time from first dosing date to the date of death. A participant who has not died will be censored at last known date alive.

99999=Not available

End point type	Secondary
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End point timeframe:

From first dosing date to the date of death (Up to approximately 67 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	395	57	
Units: Months				
median (confidence interval 95%)	16.76 (16.65 to 22.41)	10.45 (8.84 to 12.22)	26.09 (21.85 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health-Related Quality of Life (HRQoL) using Functional Assessment of Cancer Therapy-Lung (FACT-L)

End point title	Change from Baseline in Health-Related Quality of Life (HRQoL) using Functional Assessment of Cancer Therapy-Lung (FACT-L) ^[9]
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End point description:

FACT-L is a quality-of-life questionnaire which includes the Lung Cancer Subscale (LCS) that assesses the treatment impact on lung cancer related symptoms in 5 domains: Physical, social/family, emotional, and functional well-being using a 5-point scale (0=not at all) to (4=very much) added to obtain total score. The ranges of possible total scores are 0 - 136 for the FACT-L with a higher score representing better quality of life, improved symptomatology and enhanced physical/functional outcomes. According to Functional Assessment of Chronic Illness Therapy scoring guidelines, in the event of missing responses for some of the questions/items, scores will be prorated using the average of the other answers in that scale.

Baseline is defined as evaluations or events that occur before the date and time of the first dose of

study treatment.

Post treatment follow-up includes 2 visits for safety and subsequent survival follow-up every 3 months.

99999=Not available

End point type	Secondary
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End point timeframe:

From baseline and up to survival follow-up 18 (Up to approximately 67 months)

Notes:

[9] - 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 pre-specified arms planned for this endpoint.

End point values	Cohort A	Cohort B	Cohort C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	364 ^[10]	365 ^[11]	57 ^[12]	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Baseline	94.89 (± 19.33)	91.20 (± 18.45)	93.96 (± 17.28)	
Week 6	-0.84 (± 13.82)	-0.30 (± 14.87)	2.72 (± 12.95)	
Survival Follow-up 6	14.68 (± 13.58)	3.81 (± 18.59)	15.33 (± 37.71)	
Survival Follow-up 16	5.28 (± 28.19)	-18.00 (± 99999)	99999 (± 99999)	
Survival Follow-up 18	-43.33 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Notes:

[10] - Baseline= 364

Week 6= 245

Survival Follow-up 6= 22

Survival Follow-up 16= 3

Survival Follow-up 18= 1

[11] - Baseline= 365

Week 6= 244

Survival Follow-up 6=16

Survival Follow-up 16=1

Survival Follow-up 18=0

[12] - Baseline= 57

Week 6= 41

Survival Follow-up 6= 2

Survival Follow-up 16= 0

Survival Follow-up 18= 0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and AEs are assessed from first dose to 100 days post last dose (Up to approximately 29 months). Participants were assessed for deaths (all causes) from their first dose to study completion (Up to approximately 67 months).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Cohort A
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Reporting group description:

First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

Reporting group title	Cohort C
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Reporting group description:

First-line NSCLC high tumor mutational burden (H-TMB \geq 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

Reporting group title	Cohort B
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Reporting group description:

Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

Reporting group title	Cohort A1
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Reporting group description:

First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

Serious adverse events	Cohort A	Cohort C	Cohort B
Total subjects affected by serious adverse events			
subjects affected / exposed	264 / 391 (67.52%)	42 / 57 (73.68%)	282 / 395 (71.39%)
number of deaths (all causes)	294	32	334
number of deaths resulting from adverse events	101	15	159
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	81 / 391 (20.72%)	6 / 57 (10.53%)	144 / 395 (36.46%)
occurrences causally related to treatment / all	0 / 82	0 / 6	0 / 151
deaths causally related to treatment / all	0 / 73	0 / 4	0 / 134
Bladder neoplasm			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Colon neoplasm			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangiosis carcinomatosa			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Bladder cancer			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 pleural effusion			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Metastases to bone			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroma			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion malignant			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Respiratory tract neoplasm			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour compression			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 obstruction			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Brachiocephalic vein thrombosis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Deep vein thrombosis			

subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Exsanguination			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Hypotension			
subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			

subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infarction			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Vena cava thrombosis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 391 (1.02%)	1 / 57 (1.75%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Disease progression			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
General physical health deterioration			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyperthermia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Mucosal inflammation			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Fatigue			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Performance status decreased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			

subjects affected / exposed	5 / 391 (1.28%)	0 / 57 (0.00%)	7 / 395 (1.77%)
occurrences causally related to treatment / all	0 / 5	0 / 0	2 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	6 / 391 (1.53%)	2 / 57 (3.51%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 6	0 / 2	0 / 4
Oedema peripheral			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcer			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pelvic pain			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast pain			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 391 (0.26%)	2 / 57 (3.51%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Alveolitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Asthma			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Atelectasis			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Bronchial obstruction			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchostenosis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 391 (1.53%)	1 / 57 (1.75%)	7 / 395 (1.77%)
occurrences causally related to treatment / all	0 / 9	0 / 2	1 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diaphragmatic paralysis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	14 / 391 (3.58%)	2 / 57 (3.51%)	22 / 395 (5.57%)
occurrences causally related to treatment / all	1 / 14	0 / 2	0 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	5 / 391 (1.28%)	1 / 57 (1.75%)	5 / 395 (1.27%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Hypersensitivity pneumonitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Hypoxia			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Pulmonary embolism			

subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Lung disorder			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	8 / 391 (2.05%)	0 / 57 (0.00%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonitis			
subjects affected / exposed	23 / 391 (5.88%)	3 / 57 (5.26%)	17 / 395 (4.30%)
occurrences causally related to treatment / all	22 / 24	3 / 3	18 / 18
deaths causally related to treatment / all	1 / 1	0 / 0	2 / 2
Pneumothorax			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pulmonary oedema			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Respiratory distress			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	9 / 391 (2.30%)	2 / 57 (3.51%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	2 / 9	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Disorientation			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Mental status changes			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	0 / 395 (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
Product issues			

Device loosening			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Device dislocation			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Investigations			
Amylase increased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood gases abnormal			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
C-reactive protein increased			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General physical condition abnormal			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
International normalised ratio			

increased			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza B virus test positive			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Troponin increased			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic stenosis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Fall			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site impaired healing			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Infusion related reaction			
subjects affected / exposed	4 / 391 (1.02%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	4 / 4	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Wound evisceration			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Rib fracture			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 fracture			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Recall phenomenon			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 391 (0.00%)	2 / 57 (3.51%)	0 / 395 (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
Atrial fibrillation			
subjects affected / exposed	7 / 391 (1.79%)	2 / 57 (3.51%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	1 / 7	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Arrhythmia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Angina unstable			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute coronary syndrome			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 1
Cardiac failure congestive			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Cardiac arrest			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	0 / 395 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pericardial effusion			
subjects affected / exposed	6 / 391 (1.53%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Myocardial infarction			
subjects affected / exposed	3 / 391 (0.77%)	2 / 57 (3.51%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Myocarditis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiogenic shock			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Sinus tachycardia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Pericarditis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balance disorder			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Brain oedema			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Burning sensation			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Central nervous system lesion			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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 ischaemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Encephalopathy			
subjects affected / exposed	1 / 391 (0.26%)	2 / 57 (3.51%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cluster headache			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Encephalitis autoimmune			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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	3 / 391 (0.77%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Epilepsy			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Loss of consciousness			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated encephalitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Hemianopia homonymous			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Monoparesis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Motor dysfunction			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenic syndrome			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Optic neuritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Somnolence			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Paresis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Pyramidal tract syndrome			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Status epilepticus			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Syncope			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient aphasia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Vasogenic cerebral oedema			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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			
Autoimmune anaemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Anaemia			
subjects affected / exposed	2 / 391 (0.51%)	2 / 57 (3.51%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	2 / 2	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Immune thrombocytopenia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	4 / 391 (1.02%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Ophthalmoplegia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Abdominal pain upper			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Ascites			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Chronic gastritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Barrett's oesophagus			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Colitis			
subjects affected / exposed	5 / 391 (1.28%)	0 / 57 (0.00%)	6 / 395 (1.52%)
occurrences causally related to treatment / all	5 / 5	0 / 0	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Diaphragmatic hernia			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Diarrhoea			
subjects affected / exposed	7 / 391 (1.79%)	1 / 57 (1.75%)	11 / 395 (2.78%)
occurrences causally related to treatment / all	6 / 8	1 / 1	10 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gastrointestinal necrosis			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Enteritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Enterocolitis			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	0 / 395 (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
Gastric perforation			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Gastric ulcer			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Gastritis			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Dysphagia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal toxicity			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	5 / 395 (1.27%)
occurrences causally related to treatment / all	6 / 6	0 / 0	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Pancreatitis			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Mouth ulceration			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Nausea			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Oesophagitis			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	3 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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	3 / 391 (0.77%)	1 / 57 (1.75%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	1 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Stomatitis			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subileus			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary cirrhosis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Drug-induced liver injury			
subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminaemia			

subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Liver injury			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	4 / 391 (1.02%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	4 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Toxic skin eruption			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Pustular psoriasis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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 necrosis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Eosinophilic cellulitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 391 (1.02%)	0 / 57 (0.00%)	8 / 395 (2.03%)
occurrences causally related to treatment / all	2 / 4	0 / 0	3 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Chronic kidney disease			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Haematuria			
subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	0 / 395 (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
Hydronephrosis			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated nephritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	3 / 391 (0.77%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Euthyroid sick syndrome			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 thyroiditis			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocorticotrophic hormone deficiency			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	6 / 391 (1.53%)	1 / 57 (1.75%)	4 / 395 (1.01%)
occurrences causally related to treatment / all	5 / 6	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Lymphocytic hypophysitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthralgia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intervertebral disc degeneration			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Muscular weakness			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Osteonecrosis of jaw			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Osteoarthritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Osteolysis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Polymyositis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Spinal pain			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Arthritis bacterial			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Atypical pneumonia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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	2 / 391 (0.51%)	0 / 57 (0.00%)	7 / 395 (1.77%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Cellulitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Cystitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Device related infection			

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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 infectious			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Encephalitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Erysipelas			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal oesophagitis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Diverticulitis intestinal perforated			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Infection			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Infectious pleural effusion			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infective spondylitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			

subjects affected / exposed	1 / 391 (0.26%)	1 / 57 (1.75%)	0 / 395 (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
Oral candidiasis			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Orchitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumococcal sepsis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	21 / 391 (5.37%)	2 / 57 (3.51%)	26 / 395 (6.58%)
occurrences causally related to treatment / all	1 / 26	0 / 2	3 / 27
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 1
Pneumonia aspiration			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (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
Pneumonia bacterial			

subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (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
Skin infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Respiratory tract infection			
subjects affected / exposed	7 / 391 (1.79%)	0 / 57 (0.00%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	7 / 391 (1.79%)	2 / 57 (3.51%)	5 / 395 (1.27%)
occurrences causally related to treatment / all	0 / 7	0 / 2	2 / 5
deaths causally related to treatment / all	0 / 3	0 / 1	1 / 2
Septic shock			
subjects affected / exposed	5 / 391 (1.28%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Viral infection			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 391 (0.51%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Staphylococcal infection			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	4 / 391 (1.02%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	3 / 391 (0.77%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	2 / 391 (0.51%)	2 / 57 (3.51%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	2 / 395 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	2 / 391 (0.51%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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
Hypokalaemia			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	4 / 391 (1.02%)	2 / 57 (3.51%)	3 / 395 (0.76%)
occurrences causally related to treatment / all	2 / 4	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steroid diabetes			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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 lysis syndrome			
subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (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

Serious adverse events	Cohort A1		
Total subjects affected by serious adverse events			
subjects affected / exposed	149 / 198 (75.25%)		
number of deaths (all causes)	166		
number of deaths resulting from adverse events	85		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	64 / 198 (32.32%)		
occurrences causally related to treatment / all	0 / 68		
deaths causally related to treatment / all	0 / 63		

Bladder neoplasm				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cancer pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon neoplasm				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphangiosis carcinomatosa				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder cancer				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant pleural effusion				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroma				

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion malignant			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract neoplasm			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour compression			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour obstruction			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Brachiocephalic vein thrombosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			

subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Exsanguination			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subclavian vein thrombosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infarction			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			
subjects affected / exposed	0 / 198 (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	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	0 / 198 (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	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hyperthermia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Non-cardiac chest pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Performance status decreased			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	8 / 198 (4.04%)		
occurrences causally related to treatment / all	5 / 8		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Oedema peripheral			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ulcer			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Contrast media allergy			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pelvic pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Alveolitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial obstruction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchostenosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Chronic obstructive pulmonary disease				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Diaphragmatic paralysis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	9 / 198 (4.55%)			
occurrences causally related to treatment / all	1 / 10			
deaths causally related to treatment / all	0 / 3			
Haemoptysis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity pneumonitis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated lung disease				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	6 / 198 (3.03%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Lung disorder			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pleural effusion			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary oedema			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory failure			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disorientation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			

Device loosening			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device dislocation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Amylase increased			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood gases abnormal			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
C-reactive protein increased			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical condition abnormal			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
International normalised ratio			

increased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza B virus test positive				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Troponin increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic stenosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Incision site impaired healing			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Poisoning			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural complication			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound evisceration			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Recall phenomenon			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure congestive			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac tamponade			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pericardial effusion			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiopulmonary failure			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocarditis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiogenic shock			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericarditis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Balance disorder			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Brain oedema			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Burning sensation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central nervous system lesion			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral ischaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cluster headache			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolitic stroke			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis autoimmune			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Guillain-Barre syndrome			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			

subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated encephalitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemianopia homonymous			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Monoparesis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Motor dysfunction			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myasthenic syndrome			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Neurological decompensation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Optic neuritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paresis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral motor neuropathy			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyramidal tract syndrome			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient aphasia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vasogenic cerebral oedema			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Autoimmune anaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune thrombocytopenia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Ophthalmoplegia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune colitis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic gastritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Barrett's oesophagus			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Constipation			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diaphragmatic hernia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal necrosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric perforation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal toxicity			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated enterocolitis			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mouth ulceration			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stomatitis			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Rectal haemorrhage			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct stenosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biliary cirrhosis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cholangitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic haematoma			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatitis toxic			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertransaminaemia			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic skin eruption			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pustular psoriasis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin lesion			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin necrosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eosinophilic cellulitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystitis haemorrhagic			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated nephritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophysitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Euthyroid sick syndrome			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune thyroiditis			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Adrenocorticotrophic hormone deficiency			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Adrenal insufficiency			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Thyroiditis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphocytic hypophysitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Arthralgia				
subjects affected / exposed	5 / 198 (2.53%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 1			
Back pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc degeneration				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neck pain				

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteolysis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 198 (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 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polymyositis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Rhabdomyolysis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal pain			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial infection			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Colonic abscess			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis infective			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis bacterial			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related infection			

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fungal oesophagitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis intestinal perforated			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infective spondylitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung abscess			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orchitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumococcal sepsis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Sepsis			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Septic shock			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Post procedural infection			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			

subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			

subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acidosis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			

subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Steroid diabetes			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort A	Cohort C	Cohort B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	362 / 391 (92.58%)	56 / 57 (98.25%)	346 / 395 (87.59%)
Vascular disorders			
Hypotension			
subjects affected / exposed	20 / 391 (5.12%)	7 / 57 (12.28%)	12 / 395 (3.04%)
occurrences (all)	23	7	12
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	84 / 391 (21.48%)	4 / 57 (7.02%)	67 / 395 (16.96%)
occurrences (all)	104	6	83
Chills			
subjects affected / exposed	16 / 391 (4.09%)	5 / 57 (8.77%)	10 / 395 (2.53%)
occurrences (all)	16	7	10
Fatigue			
subjects affected / exposed	140 / 391 (35.81%)	24 / 57 (42.11%)	87 / 395 (22.03%)
occurrences (all)	170	31	109
Localised oedema			
subjects affected / exposed	0 / 391 (0.00%)	4 / 57 (7.02%)	0 / 395 (0.00%)
occurrences (all)	0	5	0
Malaise			
subjects affected / exposed	7 / 391 (1.79%)	3 / 57 (5.26%)	3 / 395 (0.76%)
occurrences (all)	7	3	3
Non-cardiac chest pain			
subjects affected / exposed	11 / 391 (2.81%)	5 / 57 (8.77%)	11 / 395 (2.78%)
occurrences (all)	13	5	11
Oedema peripheral			
subjects affected / exposed	39 / 391 (9.97%)	9 / 57 (15.79%)	32 / 395 (8.10%)
occurrences (all)	47	9	36
Pyrexia			
subjects affected / exposed	66 / 391 (16.88%)	7 / 57 (12.28%)	51 / 395 (12.91%)
occurrences (all)	96	8	66
Pain			
subjects affected / exposed	20 / 391 (5.12%)	5 / 57 (8.77%)	10 / 395 (2.53%)
occurrences (all)	21	5	11
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	7 / 391 (1.79%)	4 / 57 (7.02%)	8 / 395 (2.03%)
occurrences (all)	9	5	9
Pneumonitis			
subjects affected / exposed	31 / 391 (7.93%)	4 / 57 (7.02%)	18 / 395 (4.56%)
occurrences (all)	34	5	21
Nasal congestion			

subjects affected / exposed occurrences (all)	8 / 391 (2.05%) 9	3 / 57 (5.26%) 3	5 / 395 (1.27%) 8
Hypoxia subjects affected / exposed occurrences (all)	7 / 391 (1.79%) 10	8 / 57 (14.04%) 8	10 / 395 (2.53%) 11
Haemoptysis subjects affected / exposed occurrences (all)	20 / 391 (5.12%) 24	2 / 57 (3.51%) 2	21 / 395 (5.32%) 24
Dyspnoea subjects affected / exposed occurrences (all)	85 / 391 (21.74%) 97	24 / 57 (42.11%) 29	85 / 395 (21.52%) 93
Cough subjects affected / exposed occurrences (all)	98 / 391 (25.06%) 118	13 / 57 (22.81%) 14	71 / 395 (17.97%) 82
Productive cough subjects affected / exposed occurrences (all)	31 / 391 (7.93%) 37	6 / 57 (10.53%) 6	28 / 395 (7.09%) 30
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	34 / 391 (8.70%) 38	8 / 57 (14.04%) 8	17 / 395 (4.30%) 17
Depression subjects affected / exposed occurrences (all)	21 / 391 (5.37%) 24	8 / 57 (14.04%) 9	6 / 395 (1.52%) 6
Anxiety subjects affected / exposed occurrences (all)	19 / 391 (4.86%) 21	10 / 57 (17.54%) 13	11 / 395 (2.78%) 11
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	20 / 391 (5.12%) 27	6 / 57 (10.53%) 7	19 / 395 (4.81%) 27
Amylase increased subjects affected / exposed occurrences (all)	27 / 391 (6.91%) 45	3 / 57 (5.26%) 4	31 / 395 (7.85%) 61
Aspartate aminotransferase increased			

subjects affected / exposed	14 / 391 (3.58%)	6 / 57 (10.53%)	18 / 395 (4.56%)
occurrences (all)	19	7	26
Blood alkaline phosphatase increased			
subjects affected / exposed	10 / 391 (2.56%)	6 / 57 (10.53%)	20 / 395 (5.06%)
occurrences (all)	11	6	30
Blood creatinine increased			
subjects affected / exposed	18 / 391 (4.60%)	8 / 57 (14.04%)	22 / 395 (5.57%)
occurrences (all)	24	9	28
Lipase increased			
subjects affected / exposed	35 / 391 (8.95%)	3 / 57 (5.26%)	31 / 395 (7.85%)
occurrences (all)	51	5	62
Lymphocyte count decreased			
subjects affected / exposed	3 / 391 (0.77%)	3 / 57 (5.26%)	2 / 395 (0.51%)
occurrences (all)	3	6	5
Neutrophil count decreased			
subjects affected / exposed	3 / 391 (0.77%)	3 / 57 (5.26%)	4 / 395 (1.01%)
occurrences (all)	3	4	8
Weight decreased			
subjects affected / exposed	33 / 391 (8.44%)	8 / 57 (14.04%)	23 / 395 (5.82%)
occurrences (all)	35	9	23
Weight increased			
subjects affected / exposed	4 / 391 (1.02%)	5 / 57 (8.77%)	5 / 395 (1.27%)
occurrences (all)	4	5	5
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	12 / 391 (3.07%)	8 / 57 (14.04%)	8 / 395 (2.03%)
occurrences (all)	12	8	9
Infusion related reaction			
subjects affected / exposed	22 / 391 (5.63%)	4 / 57 (7.02%)	11 / 395 (2.78%)
occurrences (all)	26	5	12
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	13 / 391 (3.32%)	3 / 57 (5.26%)	8 / 395 (2.03%)
occurrences (all)	13	3	8
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	32 / 391 (8.18%) 39	7 / 57 (12.28%) 7	24 / 395 (6.08%) 24
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	2 / 391 (0.51%) 2	4 / 57 (7.02%) 6	2 / 395 (0.51%) 2
Headache subjects affected / exposed occurrences (all)	54 / 391 (13.81%) 63	10 / 57 (17.54%) 17	34 / 395 (8.61%) 39
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	53 / 391 (13.55%) 65	13 / 57 (22.81%) 15	53 / 395 (13.42%) 69
Eye disorders Dry eye subjects affected / exposed occurrences (all)	7 / 391 (1.79%) 9	4 / 57 (7.02%) 4	4 / 395 (1.01%) 4
Vision blurred subjects affected / exposed occurrences (all)	10 / 391 (2.56%) 11	3 / 57 (5.26%) 3	5 / 395 (1.27%) 5
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	33 / 391 (8.44%) 40	7 / 57 (12.28%) 11	21 / 395 (5.32%) 26
Colitis subjects affected / exposed occurrences (all)	9 / 391 (2.30%) 9	4 / 57 (7.02%) 4	3 / 395 (0.76%) 4
Constipation subjects affected / exposed occurrences (all)	69 / 391 (17.65%) 81	11 / 57 (19.30%) 12	53 / 395 (13.42%) 60
Diarrhoea subjects affected / exposed occurrences (all)	122 / 391 (31.20%) 217	23 / 57 (40.35%) 39	80 / 395 (20.25%) 118
Dry mouth subjects affected / exposed occurrences (all)	20 / 391 (5.12%) 20	3 / 57 (5.26%) 3	12 / 395 (3.04%) 12
Dysphagia			

subjects affected / exposed occurrences (all)	12 / 391 (3.07%) 12	3 / 57 (5.26%) 3	11 / 395 (2.78%) 12
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	13 / 391 (3.32%) 15	4 / 57 (7.02%) 6	3 / 395 (0.76%) 3
Nausea subjects affected / exposed occurrences (all)	97 / 391 (24.81%) 124	25 / 57 (43.86%) 34	65 / 395 (16.46%) 80
Oral pain subjects affected / exposed occurrences (all)	1 / 391 (0.26%) 1	3 / 57 (5.26%) 3	0 / 395 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	63 / 391 (16.11%) 94	11 / 57 (19.30%) 16	52 / 395 (13.16%) 61
Skin and subcutaneous tissue disorders			
Rash maculo-papular subjects affected / exposed occurrences (all)	30 / 391 (7.67%) 39	10 / 57 (17.54%) 14	16 / 395 (4.05%) 22
Rash subjects affected / exposed occurrences (all)	59 / 391 (15.09%) 81	5 / 57 (8.77%) 9	52 / 395 (13.16%) 73
Pruritus subjects affected / exposed occurrences (all)	82 / 391 (20.97%) 123	16 / 57 (28.07%) 22	79 / 395 (20.00%) 103
Erythema subjects affected / exposed occurrences (all)	10 / 391 (2.56%) 12	0 / 57 (0.00%) 0	20 / 395 (5.06%) 25
Dry skin subjects affected / exposed occurrences (all)	29 / 391 (7.42%) 30	2 / 57 (3.51%) 2	24 / 395 (6.08%) 27
Endocrine disorders			
Hypothyroidism subjects affected / exposed occurrences (all)	55 / 391 (14.07%) 60	12 / 57 (21.05%) 13	45 / 395 (11.39%) 50
Hyperthyroidism			

subjects affected / exposed occurrences (all)	31 / 391 (7.93%) 33	5 / 57 (8.77%) 5	35 / 395 (8.86%) 38
Adrenal insufficiency subjects affected / exposed occurrences (all)	9 / 391 (2.30%) 9	4 / 57 (7.02%) 4	7 / 395 (1.77%) 7
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	30 / 391 (7.67%) 31	9 / 57 (15.79%) 9	27 / 395 (6.84%) 30
Myalgia subjects affected / exposed occurrences (all)	19 / 391 (4.86%) 21	4 / 57 (7.02%) 6	15 / 395 (3.80%) 19
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	12 / 391 (3.07%) 13	7 / 57 (12.28%) 8	7 / 395 (1.77%) 8
Muscular weakness subjects affected / exposed occurrences (all)	14 / 391 (3.58%) 16	5 / 57 (8.77%) 5	15 / 395 (3.80%) 15
Back pain subjects affected / exposed occurrences (all)	51 / 391 (13.04%) 57	9 / 57 (15.79%) 10	47 / 395 (11.90%) 52
Arthritis subjects affected / exposed occurrences (all)	6 / 391 (1.53%) 6	3 / 57 (5.26%) 3	3 / 395 (0.76%) 6
Arthralgia subjects affected / exposed occurrences (all)	63 / 391 (16.11%) 76	9 / 57 (15.79%) 11	44 / 395 (11.14%) 50
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	18 / 391 (4.60%) 21	4 / 57 (7.02%) 4	23 / 395 (5.82%) 25
Pneumonia subjects affected / exposed occurrences (all)	23 / 391 (5.88%) 25	4 / 57 (7.02%) 6	17 / 395 (4.30%) 17
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	23 / 391 (5.88%) 33	6 / 57 (10.53%) 7	23 / 395 (5.82%) 25
Urinary tract infection subjects affected / exposed occurrences (all)	24 / 391 (6.14%) 30	4 / 57 (7.02%) 4	11 / 395 (2.78%) 15
Nasopharyngitis subjects affected / exposed occurrences (all)	29 / 391 (7.42%) 36	0 / 57 (0.00%) 0	14 / 395 (3.54%) 20
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	96 / 391 (24.55%) 115	22 / 57 (38.60%) 27	83 / 395 (21.01%) 94
Dehydration subjects affected / exposed occurrences (all)	26 / 391 (6.65%) 31	12 / 57 (21.05%) 12	12 / 395 (3.04%) 13
Hyperglycaemia subjects affected / exposed occurrences (all)	12 / 391 (3.07%) 15	8 / 57 (14.04%) 9	21 / 395 (5.32%) 24
Hypoalbuminaemia subjects affected / exposed occurrences (all)	8 / 391 (2.05%) 12	8 / 57 (14.04%) 10	8 / 395 (2.03%) 10
Hypocalcaemia subjects affected / exposed occurrences (all)	11 / 391 (2.81%) 17	3 / 57 (5.26%) 3	9 / 395 (2.28%) 10
Hyponatraemia subjects affected / exposed occurrences (all)	18 / 391 (4.60%) 24	12 / 57 (21.05%) 17	29 / 395 (7.34%) 34
Hypomagnesaemia subjects affected / exposed occurrences (all)	12 / 391 (3.07%) 16	6 / 57 (10.53%) 6	4 / 395 (1.01%) 4
Hypokalaemia subjects affected / exposed occurrences (all)	31 / 391 (7.93%) 56	18 / 57 (31.58%) 25	24 / 395 (6.08%) 28

Non-serious adverse events	Cohort A1		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	174 / 198 (87.88%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 198 (2.53%)		
occurrences (all)	5		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	45 / 198 (22.73%)		
occurrences (all)	55		
Chills			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	39 / 198 (19.70%)		
occurrences (all)	51		
Localised oedema			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	8 / 198 (4.04%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	14 / 198 (7.07%)		
occurrences (all)	17		
Pyrexia			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	29		
Pain			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed occurrences (all)	5 / 198 (2.53%) 7		
Pneumonitis subjects affected / exposed occurrences (all)	4 / 198 (2.02%) 5		
Nasal congestion subjects affected / exposed occurrences (all)	1 / 198 (0.51%) 1		
Hypoxia subjects affected / exposed occurrences (all)	4 / 198 (2.02%) 4		
Haemoptysis subjects affected / exposed occurrences (all)	10 / 198 (5.05%) 11		
Dyspnoea subjects affected / exposed occurrences (all)	41 / 198 (20.71%) 44		
Cough subjects affected / exposed occurrences (all)	22 / 198 (11.11%) 25		
Productive cough subjects affected / exposed occurrences (all)	13 / 198 (6.57%) 14		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	14 / 198 (7.07%) 14		
Depression subjects affected / exposed occurrences (all)	1 / 198 (0.51%) 1		
Anxiety subjects affected / exposed occurrences (all)	8 / 198 (4.04%) 9		
Investigations Alanine aminotransferase increased			

subjects affected / exposed occurrences (all)	12 / 198 (6.06%) 22		
Amylase increased subjects affected / exposed occurrences (all)	19 / 198 (9.60%) 27		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 20		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	8 / 198 (4.04%) 11		
Blood creatinine increased subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 11		
Lipase increased subjects affected / exposed occurrences (all)	18 / 198 (9.09%) 21		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 198 (0.00%) 0		
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 198 (0.51%) 1		
Weight decreased subjects affected / exposed occurrences (all)	16 / 198 (8.08%) 17		
Weight increased subjects affected / exposed occurrences (all)	2 / 198 (1.01%) 2		
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	2 / 198 (1.01%) 2		
Infusion related reaction			

subjects affected / exposed occurrences (all)	2 / 198 (1.01%) 2		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	6 / 198 (3.03%) 6		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	15 / 198 (7.58%) 17 0 / 198 (0.00%) 0 26 / 198 (13.13%) 32		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	35 / 198 (17.68%) 44		
Eye disorders Dry eye subjects affected / exposed occurrences (all) Vision blurred subjects affected / exposed occurrences (all)	1 / 198 (0.51%) 1 6 / 198 (3.03%) 6		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Colitis subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	5 / 198 (2.53%) 7 7 / 198 (3.54%) 9 26 / 198 (13.13%) 28		

Diarrhoea			
subjects affected / exposed	48 / 198 (24.24%)		
occurrences (all)	58		
Dry mouth			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	4		
Dysphagia			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	4		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	40 / 198 (20.20%)		
occurrences (all)	51		
Oral pain			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	18 / 198 (9.09%)		
occurrences (all)	25		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	9		
Rash			
subjects affected / exposed	31 / 198 (15.66%)		
occurrences (all)	45		
Pruritus			
subjects affected / exposed	32 / 198 (16.16%)		
occurrences (all)	39		
Erythema			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	7		
Dry skin			

subjects affected / exposed occurrences (all)	9 / 198 (4.55%) 9		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	14 / 198 (7.07%)		
occurrences (all)	17		
Hyperthyroidism			
subjects affected / exposed	17 / 198 (8.59%)		
occurrences (all)	17		
Adrenal insufficiency			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)	9		
Myalgia			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	5 / 198 (2.53%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	15		
Arthritis			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)	7		
Arthralgia			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	27		
Infections and infestations			

Bronchitis			
subjects affected / exposed	8 / 198 (4.04%)		
occurrences (all)	9		
Pneumonia			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	15		
Upper respiratory tract infection			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)	8		
Nasopharyngitis			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	38 / 198 (19.19%)		
occurrences (all)	46		
Dehydration			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	8		
Hyperglycaemia			
subjects affected / exposed	11 / 198 (5.56%)		
occurrences (all)	11		
Hypoalbuminaemia			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	6		
Hypocalcaemia			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)	7		
Hyponatraemia			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	18		
Hypomagnesaemia			

subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	12 / 198 (6.06%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2016	Management Algorithms updated
09 November 2016	Study design and exclusion criteria updated
27 July 2017	Study design and new study personnel updated
25 October 2017	Study design updated
04 June 2018	Endpoints for Cohort C updated
02 July 2019	Updated FACT-L collection during survival follow-up

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported