

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	
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

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

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

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) Yes Is this the baseline period? Allocation method Non-randomised - controlled Blinding used Not blinded Arms Yes Are arms mutually exclusive? 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 Experimental Arm type 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 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

Dosage and administration details: 240 mg Q2W Arm title Arm description: Second-line NSCLC: Nivolumab 240 mg IV progression, unacceptable toxicity, withdror the study ends, whichever occurs first	Cohort B J Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until rawal of consent, 24 months of treatment from the first dose,	
Arm title Arm description: Second-line NSCLC: Nivolumab 240 mg IV progression, unacceptable toxicity, withdror the study ends, whichever occurs first	/ Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until	
Arm title Arm description: Second-line NSCLC: Nivolumab 240 mg IV progression, unacceptable toxicity, withdror the study ends, whichever occurs first	/ Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until	
Arm description: Second-line NSCLC: Nivolumab 240 mg IN progression, unacceptable toxicity, withdror the study ends, whichever occurs first	/ Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until	
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Second-line NSCLC: Nivolumab 240 mg IN progression, unacceptable toxicity, withdror the study ends, whichever occurs first		
progression, unacceptable toxicity, withdr or the study ends, whichever occurs first		
Arm type		
7 unit cype	Experimental	
Investigational medicinal product name I	[pilimumab	
Investigational medicinal product code		
Other name		
Pharmaceutical forms	Infusion	
Routes of administration I	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 I	Intravenous use	
Dosage and administration details:		
240 mg Q2W		
Arm title	Cohort C	
Arm description:		
Q2W + Ipilimumab 1 mg/kg IV Q6W, star	urden (H-TMB \geq 10 mutations/MB): Nivolumab 240 mg IV ting on Day 1, until progression, unacceptable toxicity, ment from the first dose, or the study ends, whichever occurs	
Arm type	Experimental	
Investigational medicinal product name	[pilimumab	
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 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
reperenting group and	00.10.02

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
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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 values	Cohort A	Cohort A1	Cohort B
Number of subjects	391	198	395
Age Categorical			
Units: Participants			
< 65 years old	183	81	200
>= 65 and < 85 years old	206	115	195
>= 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 >= 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	

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]

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

End point timeframe:

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

- [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	

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

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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 \geq 5 mm. The appearance of one or more new lesions is also considered progression.

	1
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

[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)	

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.

 $PR = \ge 30\%$ 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 \geq 5 mm. The appearance of one or more new lesions is also considered progression. 99999=Not available

End point type	Cocondami
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)	

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[8]

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

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)

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

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

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	
Dictionary used		

nctionary 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 >= 10 mutations/MB): Nivolumab 240 mg IV O2W + Ipilimumab 1 mg/kg IV O6W, 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			l Ì
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	ĺ		ĺ

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				l
	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				ĺ
	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				ĺ
	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				ĺ
	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				İ

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 (1.05%) occurrences 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 (0.28%) occurrences causally related to treatment / all 0 / 0 0 / 0 1 / 1 deaths causally related to treatment / all 0 / 0 0 / 0 1 / 1	
treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Sudden death subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Oedema peripheral subjects affected / exposed occurrences causally related to treatment / all Oedema peripheral subjects affected / exposed occurrences causally related to treatment / all O/6 O/57 (0.00%) 1/395 (0.25) O/0 1/1	·%)
treatment / all	.%)
subjects affected / exposed 6 / 391 (1.53%) 2 / 57 (3.51%) 4 / 395 (1.03) 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 occurrences causally related to treatment / all 0 / 391 (0.00%) 0 / 57 (0.00%) 1 / 395 (0.25)	.%)
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 6 0 / 2 0 / 4 Oedema peripheral subjects affected / exposed occurrences causally related to treatment / all 0 / 0 0 / 0 1 / 1 / 1	.%)
treatment / all deaths causally related to treatment / all Oedema peripheral subjects affected / exposed occurrences causally related to treatment / all O / 6 O / 2 O / 4 O / 57 (0.00%) 1 / 395 (0.25) 0 / 0 1 / 1	
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	
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	
occurrences causally related to treatment / all	
treatment / all	5%)
deaths causally related to	
treatment / all	
Ulcer	
subjects affected / exposed 0 / 391 (0.00%) 0 / 57 (0.00%) 0 / 395 (0.00%))%)
occurrences causally related to 0 / 0 0 / 0 0 / 0 treatment / all	
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 1 / 2 0 / 0 treatment / all	
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 0 / 1 0 / 0 treatment / all	
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 1 / 1 0 / 0 0 / 0 treatment / all	
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	5%)
occurrences causally related to 0 / 0 0 / 0 0 / 1 treatment / all	

Pelvic pain	1 1		
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	j		j
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	i İ		
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			<u> </u>
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
Нурохіа			
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%
	2/2	0/0	0/0
occurrences causally related to treatment / all	,		

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	İ		

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	1		İ
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	j		
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			

Subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatm	Device loosening			
treatment / all deaths causally related to deaths causally related to deaths causally related to deat	_	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (0.00%)
Treatment / all		0 / 0	0 / 1	0 / 0
Subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatm		0 / 0	0 / 0	0 / 0
Occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O / 0	Device dislocation			
treatment / all deaths causally related to treatment / all	subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
Treatment / all		0 / 1	0 / 0	0 / 0
Amylase increased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to decorrences causally related to decorrences causally related to deaths causally related to decorrences causally related to decorrences causally related to decorrences causally related to deaths causally related to decorrences causally related to decorrences causally related to decorrences causally related to deaths causally related to deaths causally related to decorrences causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally re		0 / 0	0 / 0	0 / 0
Subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all related to treatment / all deaths causally related to deaths causally related to dea	Investigations			
Occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O/0 O/0 O/0 O/0 O/0	Amylase increased			
treatment / all deaths causally related to treatment / all	subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
Blood creatinine increased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to deaths causally related to treatment / all deaths causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally related to deaths causally related to death		1 / 1	0 / 0	2 / 2
Subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to deaths causally related to de		0 / 0	0 / 0	0 / 0
Occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all doubt concurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to deaths causa	Blood creatinine increased			
treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to deaths causally related to treatment / all deaths causally related to deaths ca	subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
treatment / all		0 / 1	0 / 0	0 / 1
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 / 1 0 / 0 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		0 / 0	0 / 0	0 / 0
occurrences causally related to treatment / all deaths causally related to treatment / all 1 / 1 0 / 0 0 / 0 C-reactive protein increased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 391 (0.00%) 0 / 57 (0.00%) 1 / 395 (0.25%) General physical condition abnormal subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to deaths causally r	Blood gases abnormal			
treatment / all deaths causally related to treatment / all	subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
C-reactive protein increased subjects affected / exposed		1 / 1	0 / 0	0 / 0
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 0 / 0 deaths causally related to treatment / all 0 / 1 0 / 0 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		0 / 0	0 / 0	0 / 0
occurrences causally related to treatment / all deaths causally related to treatment / all	C-reactive protein increased			
treatment / all deaths causally related to treatment / all deaths causally related to treatment / all General physical condition abnormal subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Oxygen saturation decreased subjects affected / exposed occurrences causally related to treatment / all Oxygen saturation decreased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all	subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
treatment / all		0 / 0	0 / 0	0 / 1
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		0 / 0	0 / 0	0 / 1
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	General physical condition abnormal			
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 1 0 / 0 0 / 0 Oxygen saturation decreased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all 0 / 0 0 / 0 0 / 0	1	2 / 391 (0.51%)	0 / 57 (0.00%)	0 / 395 (0.00%)
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 deaths causally related to treatment / all 0 / 0 0 / 0 0 / 0			-	
subjects affected / exposed		0 / 1	0 / 0	0 / 0
subjects affected / exposed	Oxygen saturation decreased			
occurrences causally related to treatment / all 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0 0 / 0		1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
deaths causally related to treatment / all 0 / 0 0 / 0 0 / 0			-	
	deaths causally related to	0 / 0	0 / 0	0 / 0
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ncreased	, ,		ı
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
ipase 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
nfluenza 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
Fransaminases 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
Froponin increased	j		
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

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	i i		
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	· · · · · · · · · · · · · · · · · · ·	•	' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '
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	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	
1	Poisoning				1
	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	i
	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				ĺ
	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				l
	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				ĺ
	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	1			ĺ

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	i İ		j
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			i i

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				ĺ
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]			

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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			[

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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
			

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	ļ]
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			ĺ
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	i I		İ
subjects affected / exposed	0 / 391 (0.00%)	1 / 57 (1.75%)	0 / 395 (0.00%)
occurrences causally related to	0/0	0 / 1	0/0
treatment / all	0 / 0	0 / 1	
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			

subjects affected / exposed	1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%
occurrences causally related to	1/1	0 / 0	0 / 0
treatment / all deaths causally related to		-	
treatment / all	0 / 0	0 / 0	0/0
strointestinal 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	j		
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	1 0,0	0,0	1 0,0

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	1			

	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	
1	Gastritis				l
	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				l
	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				l
	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				l
	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				l
	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	
١	Intestinal perforation				l
	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	į į		ĺ	

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)	l
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				ĺ
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				ĺ
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				l
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				l
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				İ

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	ĺ	ĺ	ĺ
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
1			

	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				1
1	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				
1	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				
1	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	
	Hypertransaminasaemia				

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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			i i
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	· 		i
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1 / 391 (0.26%)	0 / 57 (0.00%)	1 / 395 (0.25%)
2 / 2	0 / 0	1/1
0/0	0 / 0	0 / 0
0 / 391 (0.00%)	0 / 57 (0.00%)	0 / 395 (0.00%)
0 / 0	0 / 0	0 / 0
0 / 0	0 / 0	0 / 0
1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
0 / 1	0 / 0	0 / 0
0 / 0	0 / 0	0 / 0
0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
0 / 0	0 / 0	1/1
0 / 0	0 / 0	0 / 0
4 / 391 (1.02%)	0 / 57 (0.00%)	8 / 395 (2.03%)
2 / 4	0 / 0	3 / 9
0 / 0	0 / 0	1 / 2
0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
0 / 0	0 / 0	0 / 1
0 / 0	0 / 0	0 / 0
1 / 391 (0.26%)	0 / 57 (0.00%)	0 / 395 (0.00%)
0 / 1	0 / 0	0 / 0
0/0	0 / 0	0 / 0
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3 / 391 (0.77%)	0 / 57 (0.00%)	0 / 395 (0.00%)
0/3	0 / 0	0 / 0
0/0	0 / 0	0 / 0
	2 / 2 0 / 0 0 / 391 (0.00%) 0 / 0 0 / 0 1 / 391 (0.26%) 0 / 1 0 / 0 0 / 0 4 / 391 (0.00%) 0 / 0 4 / 391 (0.00%) 2 / 4 0 / 0 0 / 0 1 / 391 (0.00%) 0 / 0 1 / 391 (0.26%) 0 / 0 3 / 391 (0.77%) 0 / 3	2/2 0/0 0/0 0/0 0/391 (0.00%) 0/57 (0.00%) 0/0 0/0 0/0 0/0 1/391 (0.26%) 0/57 (0.00%) 0/1 0/0 0/0 0/0 0/0 0/57 (0.00%) 0/0 0/0 4/391 (1.02%) 0/57 (0.00%) 2/4 0/0 0/0 0/57 (0.00%) 0/0 0/0 1/391 (0.00%) 0/57 (0.00%) 0/0 0/0 1/391 (0.26%) 0/57 (0.00%) 0/1 0/0 3/391 (0.77%) 0/57 (0.00%) 0/3 0/0

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	ĺ		ĺ
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
Adrenocorticotropic 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	1 1		I
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	0/0	0/0	0 / 0
treatment / all			
treatment / all deaths causally related to treatment / all	0 / 0	0 / 0	0/0

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	ĺ		ĺ

subjects affected / exposed	0 / 391 (0.00%)	0 / 57 (0.00%)	1 / 395 (0.25%)
occurrences causally related to	0/0	0 / 0	0 / 1
treatment / all	, ,	σ, σ	0 / -
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	l		ĺ

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	l i		ĺ

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
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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				1
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			İ
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				1
	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				
1	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				
1	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				
1	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	

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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	l i	l
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	
/ascular 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		·
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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		ĺ

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	- , -	
гутеліа		I

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	

0 / 198 (0.00%)		
0 / 0		
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0 / 198 (0.00%)		
0 / 0		
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1 / 198 (0.51%)		
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sease subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all onnchospasm subjects affected / exposed occurrences causally related to treatment / all deaths causally related to			
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all siphragmatic paralysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	Chronic obstructive pulmonary disease		
treatment / all deaths causally related to treatment / all aphragmatic paralysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all onnchospasm subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment /		3 / 198 (1.52%)	
treatment / all aphragmatic paralysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 / 0 / 0 / 0 / 0 / 0 / 0 / 0 / 0 /		0 / 4	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 1	
occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to tre	Diaphragmatic paralysis		
treatment / all deaths causally related to treatment / all onchospasm subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	1 / 198 (0.51%)	
treatment / all		0 / 1	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all aemoptysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all oppersensitivity pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 occurrences causally related to treatment / all occurrences causally related t	Bronchospasm		
treatment / all deaths causally related to treatment / all yspnoea subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all aemoptysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ypersensitivity pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all aemoptysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0 1 / 198 (0.51%) occurrences causally related to 1 / 198 (0.51%)		0 / 0	
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treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deamoptysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all	subjects affected / exposed	9 / 198 (4.55%)	
acemoptysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ypersensitivity pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ypoxia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all		1 / 10	
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occurrences causally related to treatment / all deaths causally related to treatment / all	Haemoptysis		
treatment / all deaths causally related to treatment / all o / 0 presensitivity pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to 1 / 198 (0.51%) occurrences causally related to	subjects affected / exposed	2 / 198 (1.01%)	
ypersensitivity pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ypoxia subjects affected / exposed occurrences causally related to treatment / all yopoxia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to 1 / 198 (0.51%) occurrences causally related to		0 / 2	
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deaths causally related to treatment / all deaths causally related to treatment / all ypoxia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all nmune-mediated lung disease subjects affected / exposed occurrences causally related to 1 / 198 (0.51%) occurrences causally related to	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all 0 / 0 ypoxia subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all nmune-mediated lung disease subjects affected / exposed 1 / 198 (0.51%) occurrences causally related to 1 / 1		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all nmune-mediated lung disease subjects affected / exposed occurrences causally related to 1 / 198 (0.51%)		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all occurrences affected / exposed occurrences causally related to 1 / 198 (0.51%) 1 / 1	- Нурохіа		
deaths causally related to treatment / all 0 / 0 nmune-mediated lung disease subjects affected / exposed 1 / 198 (0.51%) occurrences causally related to 1 / 1	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all 0 / 0 nmune-mediated lung disease subjects affected / exposed 1 / 198 (0.51%) occurrences causally related to 1 / 1		0 / 0	
subjects affected / exposed $1 / 198 (0.51\%)$ occurrences causally related to $1 / 1$		0 / 0	
occurrences causally related to $\frac{1}{1}$	mmune-mediated lung disease		
	subjects affected / exposed	1 / 198 (0.51%)	
treatment / an	occurrences causally related to treatment / all	1/1	
deaths causally related to treatment / all 0 / 0		0 / 0	

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		
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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	

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		İ

ncreased	1	ı
subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	
deaths causally related to treatment / all	0 / 0	
ipase increased		
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 0	
deaths causally related to treatment / all	0/0	
iver 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	
leutrophil count decreased		Ì
subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	
deaths causally related to treatment / all	0/0	
nfluenza B virus test positive		1
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		1
subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	
deaths causally related to treatment / all	0 / 0	
ransaminases increased		
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 0	
deaths causally related to treatment / all	0 / 0	
roponin increased	į į	
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	i i	I
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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		1
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		İ
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	İ	i İ
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		1
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	j	İ
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 0	
deaths causally related to treatment / all	0 / 0	
Overdose	1 - / -	1

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	ĺ	Ì
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	i İ	İ
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	i İ	İ
subjects affected / exposed	0 / 198 (0.00%)	
	0 / 0	
occurrences causally related to treatment / all	","	1
treatment / all deaths causally related to treatment / all	0/0	

subjects affected / exposed	0 / 198 (0.00%)			1
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Recall phenomenon				Ì
subjects affected / exposed	0 / 198 (0.00%)			Ì
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			İ
Cardiac disorders				l
Atrial flutter				Ì
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			ı
Atrial fibrillation				
subjects affected / exposed	1 / 198 (0.51%)			Ì
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				Ì
subjects affected / exposed	0 / 198 (0.00%)			Ì
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				İ
subjects affected / exposed	0 / 198 (0.00%)			Ì
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable	į į		ĺ	
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	į į		ĺ	
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	į į		İ	Ì
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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	İ	İ	
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	i	İ	
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occurrences causally related to treatment / all deaths causally rela			
treatment / all deaths causally related to treatment / all deaths ca	subjects affected / exposed	0 / 198 (0.00%)	
Myocardial infarction subjects affected / exposed occurrences causally related to treatment / all deaths causally related to		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Myocarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0/0	
occurrences causally related to treatment / all deaths causally rela	Myocardial infarction		
treatment / all deaths causally related to treatment / all Myocarditis subjects affected / exposed occurrences causally related to treatment / all deaths	subjects affected / exposed	0 / 198 (0.00%)	
Myocarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Cardiogenic shock subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to deaths causally related to treatment / all		0/0	
occurrences causally related to treatment / all deaths causally related to treatment / all	Myocarditis		
treatment / all deaths causally related to treatment / all Cardiogenic shock subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Sinus tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Sinus tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0/0	
occurrences causally related to treatment / all deaths causally related to treatment / all	Cardiogenic shock		
treatment / all deaths causally related to treatment / all Sinus tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
Sinus tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all	Sinus tachycardia		
treatment / all deaths causally related to treatment / all Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0	subjects affected / exposed	0 / 198 (0.00%)	
Pericarditis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0 occurrences causally related to treatment / all o / 0 occurrences causally related to treatment / all o / 0		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all dervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all	Pericarditis		
treatment / all deaths causally related to treatment / all Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
Supraventricular tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0 0 / 0		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all dervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all dervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	Supraventricular tachycardia		
treatment / all deaths causally related to treatment / all deaths causally related to treatment / all dervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all o / 0 0 / 198 (0.00%) 0 / 0 0 / 0	subjects affected / exposed	1 / 198 (0.51%)	
treatment / all 0 / 0 dervous system disorders Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all 0 / 0 0 / 0 0 / 0		0 / 1	
Aphasia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 198 (0.00%) 0 / 0 0 / 0		0/0	
subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 deaths causally related to treatment / all 0 / 0	ervous system disorders		
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0	•		
treatment / all deaths causally related to treatment / all 0 / 0	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all 0 / 0		0 / 0	
Balance disorder		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			
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subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolic 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			
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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	į į	
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	İ	
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	i I I	
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	į į	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0/0	
deaths causally related to treatment / all	0 / 0	
Monoparesis	į į	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0/0	
deaths causally related to		

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	i i i	
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	i i	
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			l
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			I
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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	į į
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	i i
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	<u> </u>
Vertigo	
subjects affected / exposed	0 / 198 (0.00%)
occurrences causally related to treatment / all	0/0

subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatmen	Ophthalmoplegia		
treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally rel	subjects affected / exposed	0 / 198 (0.00%)	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
Abdominal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all dea		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	Gastrointestinal disorders		
occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Ascites subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all deaths causally related to	·		
treatment / all deaths causally related to treatment / all Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Ascites subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
Abdominal pain upper subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Ascites subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all of treatment / all of treatment / all occurrences causally related to treatment / all of treatment / all of treatment / all of treatment / all of treatment / all occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to occurrences causally related to o	Abdominal pain upper		
treatment / all deaths causally related to treatment / all Ascites subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
Ascites subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Colitis subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	Ascites		
treatment / all deaths causally related to treatment / all Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
Autoimmune colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all	Autoimmune colitis		
treatment / all deaths causally related to treatment / all Chronic gastritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	1 / 198 (0.51%)	
treatment / all	· •	1 / 1	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0 Barrett's oesophagus subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0 Colitis subjects affected / exposed 3 / 198 (1.52%) occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0	Chronic gastritis		
treatment / all deaths causally related to treatment / all Barrett's oesophagus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all occurrences causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all 0 / 0 Barrett's oesophagus subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 Colitis subjects affected / exposed 3 / 198 (1.52%) occurrences causally related to treatment / all 0 / 0 cocurrences causally related to treatment / all 0 / 0		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all ode of the subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ode of the subjects affected / exposed occurrences causally related to treatment / all occurrences causally related to treatment / all		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O / 0 3 / 198 (1.52%) 3 / 3 4 / 198 (1.52%)	Barrett's oesophagus		
occurrences causally related to treatment / all deaths causally related to treatment / all Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O / 0 3 / 198 (1.52%) 3 / 3 treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)	
treatment / all 0 / 0 Colitis subjects affected / exposed 3 / 198 (1.52%) occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0		0 / 0	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0		0 / 0	
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0	Colitis	İ	ĺ
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0	subjects affected / exposed	3 / 198 (1.52%)	
deaths causally related to treatment / all 0 / 0			
Constipation	deaths causally related to	0/0	
	Constipation	İ	İ

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	ĺ	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 0	
deaths causally related to treatment / all	0/0	
Enterocolitis	İ	
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	i	İ
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	i İ	I
1 Gasarie dicei	I	I

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			
1	I	I	I

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		
Chalangitis	· I		
i Cholangius		i	I
Cholangitis subjects affected / exposed	0 / 198 (0.00%)		
subjects affected / exposed occurrences causally related to	0 / 198 (0.00%) 0 / 0		
subjects affected / exposed			

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	1		-
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	İ		
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertransaminasaemia	İ		
1	I	1	I

occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all doaths causally rela				
treatment / all deaths causally related to treatment / all deaths ca	subjects affected / exposed	0 / 198 (0.00%)		
Liver disorder subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all liver injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Liver injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0		
occurrences causally related to treatment / all deaths causally related to treatment / all variety subjects affected / exposed occurrences causally related to treatment / all deaths causally relate	Liver disorder			
treatment / all deaths causally related to treatment / all Liver injury subjects affected / exposed	subjects affected / exposed	0 / 198 (0.00%)		
Liver injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Hepatotoxicity subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all		0 / 0		
occurrences causally related to treatment / all deaths causally related to treatment / all with treatment / all deaths causally related to treatment / all	Liver injury			
treatment / all deaths causally related to treatment / all Hepatotoxicity subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)		
treatment / all		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0		
occurrences causally related to treatment / all deaths causally related to treatment / all o / 0 Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all o / 0 Toxic skin eruption subjects affected / exposed o / 198 (0.00%) occurrences causally related to treatment / all o / 0 Toxic skin eruption subjects affected / exposed o / 198 (0.00%) occurrences causally related to treatment / all o / 0 Pustular psoriasis subjects affected / exposed o / 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all o / 0 Rash subjects affected / exposed o / 198 (0.51%) occurrences causally related to treatment / all deaths causally related to treatment / all o / 0	Hepatotoxicity			
treatment / all deaths causally related to treatment / all Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	subjects affected / exposed	0 / 198 (0.00%)		
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed		0 / 0		
Dermatitis acneiform subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all All Description Toxic skin eruption O / 0 0 / 198 (0.00%) 0 / 0 0 / 0 0 / 0 0 / 198 (0.00%) 0 / 0 0 / 0 0 / 198 (0.00%) 0 / 0 1 / 198 (0.51%) 0 / 0 Toxic skin eruption O / 0 1 / 198 (0.00%) 0 / 0 Toxic skin eruption O / 0 1 / 198 (0.51%) O / 0 Toxic skin eruption O / 0 1 / 198 (0.51%) O / 0 Toxic skin eruption O / 0 1 / 198 (0.51%) O / 0 Toxic skin eruption O / 0 Toxic		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	Skin and subcutaneous tissue disorders			
occurrences causally related to treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	Dermatitis acneiform			
treatment / all deaths causally related to treatment / all Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O / 0 Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all O / 0 O / 198 (0.00%) O / 0 I / 198 (0.51%) O / 0	subjects affected / exposed	0 / 198 (0.00%)		
Toxic skin eruption subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all		0 / 0		
occurrences causally related to treatment / all deaths causally related to treatment / all	Toxic skin eruption			
treatment / all deaths causally related to treatment / all Pustular psoriasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all No / 0 O / 198 (0.00%) O / 0 The streatment / all deaths causally related to treatment / all occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0 O / 0	subjects affected / exposed	0 / 198 (0.00%)		
treatment / all		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all occurrences causally related to treatment / all		0 / 0		
occurrences causally related to treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o / 0 1 / 198 (0.51%) 0 / 1 0 / 0	Pustular psoriasis			
treatment / all deaths causally related to treatment / all Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all 0 / 0 1 / 198 (0.51%) 0 / 1 0 / 0	subjects affected / exposed	0 / 198 (0.00%)		
treatment / all 0 / 0 Rash subjects affected / exposed 1 / 198 (0.51%) occurrences causally related to treatment / all deaths causally related to treatment / all o / 0 0 / 0		0 / 0		
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0		0 / 0		
occurrences causally related to treatment / all	Rash		j	
occurrences causally related to treatment / all		1 / 198 (0.51%)		
deaths causally related to treatment / all 0 / 0		_		
Rash maculo-papular	deaths causally related to	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	İ	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0/0	
deaths causally related to treatment / all	0 / 0	
Hydronephrosis		
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sul	pjects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0 / 0		
	aths causally related to atment / all	0 / 0		
Rena	l failure			
sul	ojects affected / exposed	1 / 198 (0.51%)		
	currences causally related to atment / all	0 / 1		
	aths causally related to atment / all	0 / 0		
Urina	ry tract obstruction			
sul	ojects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0 / 0		
	aths causally related to atment / all	0 / 0		
Imm	une-mediated nephritis			
sul	ojects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0 / 0		
	aths causally related to atment / all	0 / 0		
Endocrin	e disorders			
Нуро	pituitarism			
sul	ojects affected / exposed	1 / 198 (0.51%)		
	currences causally related to atment / all	1 / 1		
	aths causally related to atment / all	0 / 0		
Нуро	physitis			
sul	ojects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0 / 0		
	aths causally related to atment / all	0 / 0		
Нуре	rthyroidism			
	pjects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0 / 0		
	aths causally related to atment / all	0 / 0		
Euth	yroid sick syndrome			
	pjects affected / exposed	0 / 198 (0.00%)		
	currences causally related to atment / all	0/0		
dea	aths causally related to atment / all	0 / 0		
-	mmune thyroiditis			
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subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1 / 1	
deaths causally related to treatment / all	0 / 0	
Adrenocorticotropic hormone deficiency	<u> </u>	<u> </u>
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	I	
	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 198 (0.00%)	

Arthralgia	1	
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		1
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		İ
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	I	İ
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	İ	
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	
	i	(
Myalgia subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to	0 / 1	
treatment / all deaths causally related to	0.70	
treatment / all	0/0	I

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	į į	
subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1/1	
deaths causally related to treatment / all	1/1	
Rhabdomyolysis	į į	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0/0	
deaths causally related to treatment / all	0/0	
treatment / an] 0/0	

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		1
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	i i	İ
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	i i	i
subjects affected / exposed	2 / 198 (1.01%)	
occurrences causally related to treatment / all	1 / 2	
deaths causally related to treatment / all	0 / 0	
Bronchitis	i - ' - 	i I
subjects affected / exposed	2 / 100 /1 520/	
occurrences causally related to	3 / 198 (1.52%) 0 / 4	
treatment / all deaths causally related to	0 / 0	
treatment / all	11 / 11	

subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Bronchopulmonary aspergillosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Bronchitis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	
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Bronchopulmonary aspergillosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all classification occurrences causally related to treatment / all deaths causally related to	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 Cellulitis subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all o/ 0 Cholecystitis infective subjects affected / exposed o/ 1 / 198 (0.51%) occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 Clostridium difficile colitis subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all o/ 0 Clostridium difficile infection subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all deaths causally related to tr	
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treatment / all deaths causally related to treatment / all Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all Clostridium difficile subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Grystitis Cystitis	
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Cholecystitis infective subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	
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treatment / all deaths causally related to treatment / all Cholecystitis infective subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all	
treatment / all	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all cystitis	
occurrences causally related to treatment / all 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 Clostridium difficile infection subjects affected / exposed 0 / 198 (0.00%) occurrences 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 Bronchitis bacterial subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 Cyotitis 0 / 0 Cystitis	
treatment / all deaths causally related to treatment / all Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Bronchitis bacterial subjects affected / exposed o/ 198 (0.00%) occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all o/ 0 Cystitis	
treatment / all	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Bronchitis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all cystitis	
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treatment / all 0 / 0 Clostridium difficile infection subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 Bronchitis bacterial subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 ccurrences causally related to treatment / all 0 / 0 Cystitis	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Bronchitis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all deaths causally related to treatment / all Cystitis	
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treatment / all deaths causally related to treatment / all Bronchitis bacterial subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Cystitis	
treatment / all 0 / 0 Bronchitis bacterial subjects affected / exposed 0 / 198 (0.00%) occurrences causally related to treatment / all 0 / 0 Cystitis 0 / 0 Cystitis	
subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Cystitis	
occurrences causally related to treatment / all deaths causally related to treatment / all 0 / 0 Cystitis	
treatment / all deaths causally related to treatment / all Cystitis	
treatment / all 0 / 0 Cystitis	
subjects affected / exposed 0 / 198 (0.00%)	
occurrences causally related to treatment / all	
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		İ
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	· · · · · · · · · · · · · · · · · · ·	
Diverticultis intestinal perforated	Į.	I

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	İ	İ
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		
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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			<u> </u>
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			1
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	İ		
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			
I	I	I	I

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	į į	
subjects affected / exposed	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 0	
deaths causally related to treatment / all	0 / 0	
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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	į i	
subjects affected / exposed	1 / 198 (0.51%)	
occurrences causally related to treatment / all	1/1	
deaths causally related to treatment / all	0 / 0	
Dehydration	i i	
Deliyuration	1	I

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	1		
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	1		
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia	I		
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0/0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia	ĺ	- 	-
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	0/3		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia	İ		
1 ''	1	ı	ı

	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	
1	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	l İ	
	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			

Occurrences (all)	subjects affected / exposed	8 / 391 (2.05%)	3 / 57 (5.26%)	5 / 395 (1.27%)
subjects affected / exposed occurrences (all) 7 / 391 (1.79%) 8 / 57 (14.04%) 10 / 395 (2.53%) Haemoptysis subjects affected / exposed occurrences (all) 20 / 391 (5.12%) 2 / 57 (3.51%) 21 / 395 (5.32%) Dyspnoea subjects affected / exposed occurrences (all) 85 / 391 (21.74%) 24 / 57 (42.11%) 85 / 395 (21.52%) Cough subjects affected / exposed occurrences (all) 97 / 29 93 71 / 395 (17.97%) Cough subjects affected / exposed occurrences (all) 118 / 14 / 82 82 Productive cough subjects affected / exposed occurrences (all) 31 / 391 (7.93%) 6 / 57 (10.53%) 28 / 395 (7.09%) Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) 34 / 391 (8.70%) 8 / 57 (14.04%) 17 / 395 (4.30%) Depression subjects affected / exposed occurrences (all) 21 / 391 (5.37%) 8 / 57 (14.04%) 6 / 395 (1.52%) Anxiety subjects affected / exposed occurrences (all) 21 / 391 (4.86%) 10 / 57 (17.54%) 11 / 395 (2.78%) Alanine aminotransferase increased subjects affected / exposed occurrences (all) 27 / 391 (6.91%) 6 / 57 (10.53%) 19 / 395 (4.81%) Amylase increased subjects affected / exposed occurrences (all) 27 / 391 (6.91%) 3 / 57 (5.26%	occurrences (all)	9	3	8
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subjects affected / exposed occurrences (all) 20 / 391 (5.12%) 2 / 57 (3.51%) 21 / 395 (5.32%) Dyspnoea subjects affected / exposed occurrences (all) 85 / 391 (21.74%) 24 / 57 (42.11%) 85 / 395 (21.52%) Cough subjects affected / exposed occurrences (all) 98 / 391 (25.06%) 13 / 57 (22.81%) 71 / 395 (17.97%) Productive cough subjects affected / exposed occurrences (all) 31 / 391 (7.93%) 6 / 57 (10.53%) 28 / 395 (7.09%) Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) 34 / 391 (8.70%) 8 / 57 (14.04%) 17 / 395 (4.30%) Depression subjects affected / exposed occurrences (all) 21 / 391 (5.37%) 8 / 57 (14.04%) 6 / 395 (1.52%) Anxiety subjects affected / exposed occurrences (all) 24 9 6 6 10 / 57 (17.54%) 11 / 395 (2.78%) Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) 27 7 27 Amylase increased subjects affected / exposed occurrences (all) 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) Aspartate aminotransferase 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%)		10	Ü	11
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Dyspnoea subjects affected / exposed occurrences (all) 97 29 93 Cough subjects affected / exposed occurrences (all) 118 14 82 Productive cough subjects affected / exposed occurrences (all) 37 6 71 / 395 (17.97%) 6 / 57 (10.53%) 30 Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) 38 8 17 Depression subjects affected / exposed occurrences (all) 38 8 17 Depression subjects affected / exposed occurrences (all) 38 8 / 57 (14.04%) 6 / 395 (1.52%) 6 / 395 (1.52%) 6 / 395 (1.52%) 7 / 395 (4.30%)				
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Cough Subjects affected / exposed 98 / 391 (25.06%) 13 / 57 (22.81%) 71 / 395 (17.97%)	Dyspnoea			
Cough subjects affected / exposed occurrences (all) 118 14 82 Productive cough subjects affected / exposed occurrences (all) 37 6 30 Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) 38 8 17 Depression subjects affected / exposed occurrences (all) 24 9 6 Anxiety subjects affected / exposed occurrences (all) 21 11 11 Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) 27 7 27 Amylase increased subjects affected / exposed occurrences (all) 45 4 61 Aspartate aminotransferase	subjects affected / exposed	85 / 391 (21.74%)	24 / 57 (42.11%)	85 / 395 (21.52%)
subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase	occurrences (all)	97	29	93
subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Begin to be a subject of affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase	Cough			
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subjects affected / exposed occurrences (all) 31 / 391 (7.93%) 6 / 57 (10.53%) 28 / 395 (7.09%) 37 6 30 Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) 34 / 391 (8.70%) 8 / 57 (14.04%) 17 / 395 (4.30%) 8 / 57 (14.04%) 17 / 395 (4.30%) 6 / 395 (1.52%) 6 / 3				
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Anxiety subjects affected / exposed occurrences (all) Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) 21 Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) 27 Amylase increased subjects affected / exposed occurrences (all) 45 Aspartate aminotransferase	subjects affected / exposed	21 / 391 (5.37%)	8 / 57 (14.04%)	6 / 395 (1.52%)
subjects affected / exposed 19 / 391 (4.86%) 10 / 57 (17.54%) 11 / 395 (2.78%) occurrences (all) 21 13 11 Investigations Alanine aminotransferase increased subjects affected / exposed 20 / 391 (5.12%) 6 / 57 (10.53%) 19 / 395 (4.81%) occurrences (all) 27 7 27 Amylase increased subjects affected / exposed occurrences (all) 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) occurrences (all) 45 4 61 Aspartate aminotransferase	occurrences (all)	24	9	6
subjects affected / exposed 19 / 391 (4.86%) 10 / 57 (17.54%) 11 / 395 (2.78%) occurrences (all) 21 13 11 Investigations Alanine aminotransferase increased subjects affected / exposed 20 / 391 (5.12%) 6 / 57 (10.53%) 19 / 395 (4.81%) occurrences (all) 27 7 27 Amylase increased subjects affected / exposed occurrences (all) 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) occurrences (all) 45 4 61 Aspartate aminotransferase	Anxiety			
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed subjects affected / exposed occurrences (all) Aspartate aminotransferase	·	19 / 391 (4.86%)	10 / 57 (17.54%)	11 / 395 (2.78%)
Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) 20 / 391 (5.12%) 27	occurrences (all)	21	13	11
Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) 20 / 391 (5.12%) 27	Investigations			
occurrences (all) 27 Amylase increased subjects affected / exposed occurrences (all) 45 Aspartate aminotransferase	_			
Amylase increased subjects affected / exposed 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) occurrences (all) 45 4 61 Aspartate aminotransferase	subjects affected / exposed	20 / 391 (5.12%)	6 / 57 (10.53%)	19 / 395 (4.81%)
subjects affected / exposed 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) occurrences (all) 45 4 61 Aspartate aminotransferase 61	occurrences (all)	27	7	27
subjects affected / exposed 27 / 391 (6.91%) 3 / 57 (5.26%) 31 / 395 (7.85%) occurrences (all) 45 4 61 Aspartate aminotransferase 61	Amylace increased			
occurrences (all) Aspartate aminotransferase 61	1	27 / 391 (6 91%)	3 / 57 (5.26%)	31 / 395 <i>(</i> 7 85%)
Aspartate aminotransferase				
			·	
	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		= / F= /40 000/)	0.4.4.005.45.0004
	32 / 391 (8.18%)	7 / 57 (12.28%)	24 / 395 (6.08%)
occurrences (all)	39	7	24
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 391 (0.51%)	4 / 57 (7.02%)	2 / 395 (0.51%)
occurrences (all)	2	6	2
Headache			
subjects affected / exposed	54 / 391 (13.81%)	10 / 57 (17.54%)	34 / 395 (8.61%)
occurrences (all)	63	17	39
,	03	17	33
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed	F2 / 201 /12 FF0/ \	12 / 57 /22 010/ \	F2 / 20F / 12 420/ \
occurrences (all)	53 / 391 (13.55%)	13 / 57 (22.81%)	53 / 395 (13.42%)
occurrences (aii)	65	15	69
Eye disorders			
Dry eye			
subjects affected / exposed	7 / 391 (1.79%)	4 / 57 (7.02%)	4 / 395 (1.01%)
occurrences (all)	9	4	4
Vision blurred			
subjects affected / exposed	10 / 391 (2.56%)	3 / 57 (5.26%)	5 / 395 (1.27%)
occurrences (all)	11	3	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	33 / 391 (8.44%)	7 / 57 (12.28%)	21 / 395 (5.32%)
occurrences (all)	40	11	26
Colitis			
subjects affected / exposed	9 / 391 (2.30%)	4 / 57 (7.02%)	3 / 395 (0.76%)
occurrences (all)	1		
Cocan checo (an)	9	4	4
Constipation			
subjects affected / exposed	69 / 391 (17.65%)	11 / 57 (19.30%)	53 / 395 (13.42%)
occurrences (all)	81	12	60
Diarrhoea			
subjects affected / exposed	122 / 391 (31.20%)	23 / 57 (40.35%)	80 / 395 (20.25%)
occurrences (all)	217	39	118
(3.1.)	21/	33	110
Dry mouth			
subjects affected / exposed	20 / 391 (5.12%)	3 / 57 (5.26%)	12 / 395 (3.04%)
occurrences (all)	20	3	12
(,	20	3	

subjects affected / exposed	12 / 391 (3.07%)	3 / 57 (5.26%)	11 / 395 (2.78%)
occurrences (all)	12	3	12
Gastrooesophageal reflux disease subjects affected / exposed	12 / 201 /2 220/ \	4 / 57 /7 020/)	2 / 205 (0.76%)
occurrences (all)	13 / 391 (3.32%)	4 / 57 (7.02%)	3 / 395 (0.76%)
occurrences (aii)	15	6	3
Nausea			
subjects affected / exposed	97 / 391 (24.81%)	25 / 57 (43.86%)	65 / 395 (16.46%)
occurrences (all)	124	34	80
Oral pain			
subjects affected / exposed	1 / 391 (0.26%)	3 / 57 (5.26%)	0 / 395 (0.00%)
occurrences (all)	1	3	0
	_	-	
Vomiting			
subjects affected / exposed	63 / 391 (16.11%)	11 / 57 (19.30%)	52 / 395 (13.16%)
occurrences (all)	94	16	61
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	30 / 391 (7.67%)	10 / 57 (17.54%)	16 / 395 (4.05%)
occurrences (all)	39	14	22
Rash			
subjects affected / exposed	59 / 391 (15.09%)	5 / 57 (8.77%)	52 / 395 (13.16%)
occurrences (all)	81	9	73
Pruritus			
subjects affected / exposed	82 / 391 (20.97%)	16 / 57 (28.07%)	79 / 395 (20.00%)
occurrences (all)	123	22	103
Erythema			
subjects affected / exposed	10 / 391 (2.56%)	0 / 57 (0.00%)	20 / 395 (5.06%)
occurrences (all)	12	0	25
Dry skin			
subjects affected / exposed	29 / 391 (7.42%)	2 / 57 (3.51%)	24 / 395 (6.08%)
occurrences (all)	30	2 / 37 (3.3170)	27
	30	۷	21
Endocrine disorders			
Hypothyroidism subjects affected / exposed	FF / 201 /14 070/	12 / 57 /24 050/	45 / 205 / 44 200/
	55 / 391 (14.07%)	12 / 57 (21.05%)	45 / 395 (11.39%)
occurrences (all)	60	13	50
Hyperthyroidism			

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

subjects affected / exposed	23 / 391 (5.88%)	6 / 57 (10.53%)	23 / 395 (5.82%)
occurrences (all)	33	7	25
Urinary tract infection			
subjects affected / exposed	24 / 391 (6.14%)	4 / 57 (7.02%)	11 / 395 (2.78%)
occurrences (all)	30	4	15
Nasopharyngitis			
subjects affected / exposed	29 / 391 (7.42%)	0 / 57 (0.00%)	14 / 395 (3.54%)
occurrences (all)	36	0	20
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	96 / 391 (24.55%)	22 / 57 (38.60%)	83 / 395 (21.01%)
occurrences (all)	115	27	94
Dehydration			
subjects affected / exposed	26 / 391 (6.65%)	12 / 57 (21.05%)	12 / 395 (3.04%)
occurrences (all)	31	12	13
Hyperglycaemia			
subjects affected / exposed	12 / 391 (3.07%)	8 / 57 (14.04%)	21 / 395 (5.32%)
occurrences (all)	15	9	24
Hypoalbuminaemia			
subjects affected / exposed	8 / 391 (2.05%)	8 / 57 (14.04%)	8 / 395 (2.03%)
occurrences (all)	12	10	10
Hypocalcaemia			
subjects affected / exposed	11 / 391 (2.81%)	3 / 57 (5.26%)	9 / 395 (2.28%)
occurrences (all)	17	3	10
Hyponatraemia			
subjects affected / exposed	18 / 391 (4.60%)	12 / 57 (21.05%)	29 / 395 (7.34%)
occurrences (all)	24	17	34
Hypomagnesaemia			
subjects affected / exposed	12 / 391 (3.07%)	6 / 57 (10.53%)	4 / 395 (1.01%)
occurrences (all)	16	6	4
Hypokalaemia			
subjects affected / exposed	31 / 391 (7.93%)	18 / 57 (31.58%)	24 / 395 (6.08%)
occurrences (all)	56	25	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	
Coodin enece (un)	2	
Fatigue		
subjects affected / exposed	39 / 198 (19.70%)	
occurrences (all)	51	
	51	
Localised oedema		
subjects affected / exposed	1 / 198 (0.51%)	
occurrences (all)	1	
Malaise		
subjects affected / exposed	1 / 100 /0 510/	
	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		

1	I
subjects affected / exposed	5 / 198 (2.53%)
occurrences (all)	7
Do a como a militira	
Pneumonitis subjects affected / exposed	4 / 100 /2 020/)
	4 / 198 (2.02%)
occurrences (all)	5
Nasal congestion	
subjects affected / exposed	1 / 198 (0.51%)
	}
occurrences (all)	1
 Hypoxia	
subjects affected / exposed	4 / 198 (2.02%)
occurrences (all)	
decarrences (un)	4
 Haemoptysis	
subjects affected / exposed	10 / 198 (5.05%)
occurrences (all)	11
Dyspnoea	
subjects affected / exposed	41 / 198 (20.71%)
occurrences (all)	44
Cough	
subjects affected / exposed	22 / 198 (11.11%)
occurrences (all)	25
Productive cough	
subjects affected / exposed	13 / 198 (6.57%)
occurrences (all)	14
Development of the state of the	
Psychiatric disorders Insomnia	
subjects affected / exposed	14 / 100 /7 070/ \
	14 / 198 (7.07%)
occurrences (all)	14
Depression	
subjects affected / exposed	1 / 198 (0.51%)
occurrences (all)	
occurrences (an)	1
Anxiety	
subjects affected / exposed	8 / 198 (4.04%)
occurrences (all)	9
00000.000 (4)	9
Investigations	
Alanine aminotransferase increased	
	•

subjects affected / exposed	12 / 198 (6.06%)
occurrences (all)	22
Amylase increased	
subjects affected / exposed	19 / 198 (9.60%)
occurrences (all)	27
Aspartate aminotransferase increased	
subjects affected / exposed	11 / 198 (5.56%)
occurrences (all)	20
Blood alkaline phosphatase increased	
subjects affected / exposed	8 / 198 (4.04%)
occurrences (all)	11
Blood creatinine increased	
subjects affected / exposed	11 / 198 (5.56%)
occurrences (all)	11
Lipase increased	
subjects affected / exposed	18 / 198 (9.09%)
occurrences (all)	21
Lymphopyto sount document	
Lymphocyte count decreased subjects affected / exposed	0 / 109 /0 009/)
	0 / 198 (0.00%)
occurrences (all)	0
Neutrophil count decreased	
subjects affected / exposed	1 / 198 (0.51%)
occurrences (all)	1
	<u> </u>
Weight decreased	
subjects affected / exposed	16 / 198 (8.08%)
occurrences (all)	17
Wainkt in an and	
Weight increased	2 / 100 / 1 010/
subjects affected / exposed	2 / 198 (1.01%)
occurrences (all)	2
Injury, poisoning and procedural complications Fall	
subjects affected / exposed	2 / 198 (1.01%)
occurrences (all)	2
Infusion related reaction	

subjects affected / exposed	2 / 198 (1.01%)		
occurrences (all)	2		
Cardiac disorders Atrial fibrillation			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)	6		
	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	17		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	26 / 198 (13.13%)		
occurrences (all)	32		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	35 / 198 (17.68%)		
occurrences (all)	44		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	6 / 198 (3.03%)		
occurrences (all)			
occurrences (an)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 198 (2.53%)		
occurrences (all)	7		
Colitis			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)			
1 Occurrences (an)	4	-,	
occurrences (un)	9		
Constipation	9		
	26 / 198 (13.13%)		
Constipation			

Diarrhoea	
subjects affected / exposed	48 / 198 (24.24%)
occurrences (all)	58
Day and the	
Dry mouth subjects affected / exposed	4 / 198 (2.02%)
occurrences (all)	
occurrences (un)	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	9 / 198 (4.55%)	
occurrences (all)	9	
Endocrine disorders Hypothyroidism		
subjects affected / exposed	14 / 198 (7.07%)	
occurrences (all)	17	
,	1,	
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	
,	J	
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	
Authoration		
Arthralgia subjects affected / exposed	25 / 100 /12 (20/)	
	25 / 198 (12.63%)	
occurrences (all)	27	i

Bronchitis	[
subjects affected / exposed	8 / 198 (4.04%)
occurrences (all)	9
	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)	
occarrences (an)	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)	
occurrences (an)	7
Hyponatraemia	
subjects affected / exposed	13 / 198 (6.57%)
occurrences (all)	18
Hypomagnesaemia	

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