Clinical trial results:
Non-Comparative, Open-Label, Multiple Cohort, Phase 1/2 Study of Nivolumab Monotherapy and Nivolumab Combination Therapy in Subjects with Virus-Positive and Virus-Negative Solid Tumors

Summary

EudraCT number	2015-000230-29
Trial protocol	NL DE BE GB ES
Global end of trial date	24 October 2022

Results information

Result version number	v1 (current)
This version publication date	01 November 2023
First version publication date	01 November 2023

Trial information

Trial identification

Sponsor protocol code	CA209-358

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	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate safety and efficacy of Nivolumab monotherapy and Nivolumab combination therapy in subjects with viral positive and viral negative multiple tumor types

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	13 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Netherlands: 32
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 15
Country: Number of subjects enrolled	Spain: 97
Country: Number of subjects enrolled	United Kingdom: 55
Country: Number of subjects enrolled	United States: 239
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Mexico: 27
Worldwide total number of subjects	578
EEA total number of subjects	215

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	400
From 65 to 84 years	170
85 years and over	8

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

578 participants treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Metastatic Monotherapy

Arm description:

Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg every 2 weeks for a maximum of 24 months

Arm title	Metastatic Combo A

Arm description:

Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

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

Dosage and administration details:

1 mg/kg every 6 weeks for a maximum of 24 months

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg every 2 weeks for a maximum of 24 months

Arm title	Metastatic Combo B

Arm description:

Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4

doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

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

Dosage and administration details:

3 mg/kg every 3 weeks for 4 doses

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg every 3 weeks for 4 doses followed by 240 mg every 2 weeks for a maximum of 24 months

Arm title	Metastatic Combo C

Arm description:

Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Arm type	Experimental
Investigational medicinal product name	Relatlimab
Investigational medicinal product code	BMS-986016
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

80 mg every 2 weeks for a maximum of 24 months

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg every 2 weeks for a maximum of 24 months

Arm title	Metastatic Combo D

Arm description:

Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

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

Dosage and administration details:

16 mg/kg weekly for the first 8 weeks and then every 2 weeks from weeks 9-24

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Starting at week 3, 240 mg every 2 weeks and then starting at week 25, 480 mg every 4 weeks for a maximum of 24 months

Arm title	Neoadjuvant

Arm description:

Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 mg for 2 doses, on Day 1 and Day 15

Number of subjects in period 1	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B
Started	113	195	133
Completed	0	0	0
Not completed	113	195	133
Consent withdrawn by subject	4	-	3
Disease progression	73	111	62
Study drug toxicity	11	33	31
Maximum clinical benefit	3	-	1
Adverse event unrelated to study drug	9	11	7
Other reasons	7	32	23
Lost to follow-up	-	-	2
Participant request to discontinue study treatment	6	8	4

Number of subjects in period 1	Metastatic Combo C	Metastatic Combo D	Neoadjuvant
Started	8	6	123
Completed	0	0	116
Not completed	8	6	7
Consent withdrawn by subject	-	-	2
Disease progression	7	4	2
Study drug toxicity	-	-	2
Maximum clinical benefit	-	-	-

Adverse event unrelated to study drug	-	1	-
Other reasons	1	1	1
Lost to follow-up	-	-	-
Participant request to discontinue study treatment	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Metastatic Monotherapy
Reporting group description:	
Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo A
Reporting group description:	
Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo B
Reporting group description:	
Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo C
Reporting group description:	
Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo D
Reporting group description:	
Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Neoadjuvant
Reporting group description:	
Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15	

Reporting group values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B
Number of subjects	113	195	133
Age categorical Units:			
Age Continuous Units: years			
arithmetic mean	57.4	57.5	48.2
standard deviation	± 13.5	± 13.2	± 12.3
Sex: Female, Male Units: Participants			
Female	39	85	129
Male	74	110	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	14	31	10

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	6	5
White	86	147	115
More than one race	0	0	0
Unknown or Not Reported	8	11	1

Reporting group values	Metastatic Combo C	Metastatic Combo D	Neoadjuvant
Number of subjects	8	6	123
Age categorical			
Units:			

Age Continuous			
Units: years			
arithmetic mean	59.0	66.5	62.0
standard deviation	± 7.6	± 15.3	± 12.7
Sex: Female, Male			
Units: Participants			
Female	1	3	59
Male	7	3	64
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	2
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	3
White	8	6	113
More than one race	0	0	0
Unknown or Not Reported	0	0	4

Reporting group values	Total		
Number of subjects	578		
Age categorical			
Units:			

Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	316		
Male	262		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	6		
Asian	56		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	17		
White	475		

More than one race	0		
Unknown or Not Reported	24		

End points

End points reporting groups

Reporting group title	Metastatic Monotherapy
Reporting group description:	
Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo A
Reporting group description:	
Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo B
Reporting group description:	
Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo C
Reporting group description:	
Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Metastatic Combo D
Reporting group description:	
Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first	
Reporting group title	Neoadjuvant
Reporting group description:	
Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15	

Primary: Neoadjuvant: Number of Participants with Drug-Related Select Adverse Events (AEs)

End point title	Neoadjuvant: Number of Participants with Drug-Related Select Adverse Events (AEs)[1][2]
End point description:	
Number of participants with any grade of drug-related select adverse events (AEs) including endocrine, gastrointestinal, hepatic, pulmonary, renal, skin, and hypersensitivity AEs in Neoadjuvant cohort	
End point type	Primary
End point timeframe:	
From first dose to 30 days post last dose (Up to 2 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 analysis 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 specified arms planned for this endpoint

End point values	Neoadjuvant			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Participants				
Endocrine AEs	3			
Gastrointestinal AEs	4			
Hepatic AEs	3			
Pulmonary AEs	0			
Renal AEs	0			
Skin AEs	9			
Hypersensitivity/Infusion Reaction AEs	5			

Statistical analyses

No statistical analyses for this end point

Primary: Neoadjuvant: Rate of Surgery Delay

End point title	Neoadjuvant: Rate of Surgery Delay[3][4]

End point description:

Rate of surgery delay is defined as the percentage of participants in the neoadjuvant cohort with surgery delayed > 4 weeks from the planned surgery date or planned start date for chemoradiation due to a drug-related adverse event.
Participants with the following diseases will be assessed:
1. HPV positive squamous cell carcinoma of the Head and Neck (SCCHN);
2. HPV negative SCCHN;
3. Cervical Carcinoma;
4. Vaginal/Vulvar Carcinoma;
5. Merkel Cell Carcinoma

End point type	Primary

End point timeframe:

Day 29

Notes:

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

End point values	Neoadjuvant			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: Percentage of participants				
number (confidence interval 95%)				
HPV positive SCCHN	0 (0 to 13.7)			
HPV negative SCCHN	0 (0 to 13.7)			
Cervical Carcinoma	7.7 (0.2 to 36.0)			
Vaginal/Vulvar Carcinoma	0 (0.0 to 26.5)			
Merkel Cell Carcinoma	2.7 (0.1 to 14.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Neoadjuvant: Number of Participants with Drug-Related Serious Adverse Events (SAEs)

End point title	Neoadjuvant: Number of Participants with Drug-Related Serious Adverse Events (SAEs)[5][6]

End point description:

Number of participants with any grade of drug-related serious adverse events (SAEs) in Neoadjuvant cohort

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (Up to 2 months)

Notes:

[5] - 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 analysis planned for this endpoint

[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 specified arms planned for this endpoint

End point values	Neoadjuvant			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Participants	6			

Statistical analyses

No statistical analyses for this end point

Primary: Metastatic: Investigator-Assessed Objective Response Rate (ORR)

End point title	Metastatic: Investigator-Assessed Objective Response Rate (ORR)[7][8]

End point description:

Objective response rate (ORR) is defined as the percentage of participants with a best overall response (BOR) of confirmed complete response (CR) or partial response (PR) using RECIST 1.1 criteria. An ORR in excess of 10% will be considered of clinical interest, and an ORR of 25% or greater will be considered of strong clinical interest.
Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Participants with the following diseases will be assessed:
1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;

4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)
99999=NA

End point type	Primary

End point timeframe:

From the date of first dose to the date of the initial objectively documented tumor progression or the date of the last tumor assessment prior to subsequent therapy (Up to 72 months)

Notes:

[7] - 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 analysis planned for this endpoint

[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 specified arms planned for this endpoint

End point values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B	Metastatic Combo C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	195	133	8
Units: Percentage of participants				
number (confidence interval 95%)				
EBV positive related gastric cancer	14.3 (1.8 to 42.8)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
HPV positive SCCHN	11.5 (2.4 to 30.2)	31.0 (17.6 to 47.1)	99999 (99999 to 99999)	0 (0.0 to 36.9)
Other anogenital HPV associated cancers	99999 (99999 to 99999)	34.8 (16.4 to 57.3)	28.6 (11.3 to 52.2)	99999 (99999 to 99999)
SCCHN I-O naive	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cervical	26.3 (9.1 to 51.2)	31.1 (18.2 to 46.6)	40.0 (25.7 to 55.7)	99999 (99999 to 99999)
Cervical first line	99999 (99999 to 99999)	99999 (99999 to 99999)	36.4 (22.4 to 52.2)	99999 (99999 to 99999)
Cervical second line	99999 (99999 to 99999)	99999 (99999 to 99999)	39.1 (19.7 to 61.5)	99999 (99999 to 99999)
Vaginal/Vulvar	20.0 (0.5 to 71.6)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
MCC	64.0 (42.5 to 82.0)	58.1 (42.1 to 73.0)	99999 (99999 to 99999)	99999 (99999 to 99999)
NPC	16.7 (4.7 to 37.4)	26.2 (13.9 to 42.0)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Metastatic Combo D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of participants				
number (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)			
HPV positive SCCHN	99999 (99999 to 99999)			
Other anogenital HPV associated cancers	99999 (99999 to 99999)			

SCCHN I-O naive	16.7 (0.4 to 64.1)			
Cervical	99999 (99999 to 99999)			
Cervical first line	99999 (99999 to 99999)			
Cervical second line	99999 (99999 to 99999)			
Vaginal/Vulvar	99999 (99999 to 99999)			
MCC	99999 (99999 to 99999)			
NPC	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Metastatic: Investigator-Assessed Duration of Response (DoR)

End point title	Metastatic: Investigator-Assessed Duration of Response

End point description:

Duration of response (DoR) is defined as the time from first confirmed response (complete response or partial response) to the date of the initial objectively documented tumor progression as determined per investigator assessment using RECIST 1.1 criteria or death due to any cause, whichever occurs first.
Participants with the following diseases will be assessed:
1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)
NOTE: "Cervical, Randomized" and "Cervical, Pooled" are not mutually exclusive categories.
99999=NA

End point type	Secondary

End point timeframe:

From first confirmed response (complete response or partial response) to the date of the initial objectively documented tumor progression or death due to any cause, whichever occurs first (Up to 83 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 specified arms planned for this endpoint

End point values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B	Metastatic Combo C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30[10]	72[11]	50[12]	0[13]
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	(to)
HPV positive SCCHN	44.25 (24.90 to 99999)	34.46 (10.45 to 99999)	99999 (99999 to 99999)	(to)
Other anogenital HPV associated cancers	99999 (99999 to 99999)	18.23 (3.68 to 27.93)	3.71 (3.58 to 99999)	(to)

SCCHN I-O naive	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	(to)
Cervical, Randomized	99999 (35.29 to 99999)	99999 (8.67 to 99999)	34.07 (15.28 to 99999)	(to)
Cervical, Pooled	99999 (99999 to 99999)	99999 (99999 to 99999)	34.07 (15.28 to 99999)	(to)
Vaginal/Vulvar	4.96 (-99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	(to)
MCC	60.62 (16.72 to 99999)	25.86 (10.38 to 99999)	99999 (99999 to 99999)	(to)
NPC	9.46 (3.68 to 99999)	19.63 (5.55 to 99999)	99999 (99999 to 99999)	(to)

Notes:

[10] - EBV N=2
HPV N=3
Other HPV N=0
SCCHN N=0
Cervical, R N=5
Cervical, P N=0
Vaginal N=1
MCC N=15
NPC N=4

[11] - EBV N=0
HPV N=13
Other HPV N=8
SCCHN N=0
Cerv. R N=14
Cerv. P N=0
Vaginal N=0
MCC N=25
NPC N=12

[12] - EBV N=0
HPV N=0
Other HPV N=5
SCCHNN=0
Cervical R N=18
Cervical P N=45
Vaginal N=0
MCC N=0
NPC N=0

[13] - 0 complete and partial responders

End point values	Metastatic Combo D			
Subject group type	Reporting group			
Number of subjects analysed	1[14]			
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)			
HPV positive SCCHN	99999 (99999 to 99999)			
Other anogenital HPV associated cancers	99999 (99999 to 99999)			
SCCHN I-O naive	99999 (99999 to 99999)			
Cervical, Randomized	99999 (99999 to 99999)			
Cervical, Pooled	99999 (99999 to 99999)			
Vaginal/Vulvar	99999 (99999 to 99999)			
MCC	99999 (99999 to 99999)			

NPC	99999 (99999 to 99999)			

Notes:

[14] - EBV N=0
HPV N=0
Other HPV N=0
SCCHN N=1
Cervical, R N=0
Cervical, P N=0
Vaginal N=0
MCC N=0
NPC N=0

Statistical analyses

No statistical analyses for this end point

Secondary: Metastatic: Overall Survival (OS)

End point title	Metastatic: Overall Survival (OS)[15]

End point description:

Overall survival (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. Participants with the following diseases will be assessed:
1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)
99999=NA

End point type	Secondary

End point timeframe:

From the first dosing date to the date of death (Up to 83 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only specified arms planned for this endpoint

End point values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B	Metastatic Combo C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	195	133	8
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	9.99 (3.09 to 30.13)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
HPV positive SCCHN	20.44 (13.90 to 36.50)	17.08 (9.49 to 26.78)	99999 (99999 to 99999)	8.84 (2.50 to 35.06)
Other anogenital HPV associated cancers	99999 (99999 to 99999)	12.12 (6.83 to 29.54)	14.06 (4.37 to 30.59)	99999 (99999 to 99999)
SCCHN I-O naive	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cervical, Randomized	21.55 (8.25 to 44.85)	17.12 (10.22 to 34.79)	22.74 (14.62 to 32.82)	99999 (99999 to 99999)
Vaginal/Vulvar	10.28 (3.88 to 23.72)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
MCC	80.66 (23.26 to 99999)	29.83 (8.51 to 48.33)	99999 (99999 to 99999)	99999 (99999 to 99999)
NPC	22.74 (12.62 to 35.29)	23.66 (16.82 to 41.43)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Metastatic Combo D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)			
HPV positive SCCHN	99999 (99999 to 99999)			
Other anogenital HPV associated cancers	99999 (99999 to 99999)			
SCCHN I-O naive	4.21 (1.68 to 99999)			
Cervical, Randomized	99999 (99999 to 99999)			
Vaginal/Vulvar	99999 (99999 to 99999)			
MCC	99999 (99999 to 99999)			
NPC	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Metastatic: Investigator-Assessed Progression-Free Survival (PFS)

End point title	Metastatic: Investigator-Assessed Progression-Free Survival (PFS)[16]

End point description:

Investigator-assessed progression free survival (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 1.1), or death due to any cause, whichever occurs first. Participants with the following diseases will be assessed:
1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)
99999=NA

End point type	Secondary

End point timeframe:

From the first dosing date to the date of the first documented tumor progression or death due to any cause, whichever occurs first (Up to 83 months)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only specified arms planned for this endpoint

End point values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B	Metastatic Combo C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	195	133	8
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	2.94 (1.05 to 3.75)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
HPV positive SCCHN	3.25 (1.84 to 6.93)	3.71 (1.77 to 6.80)	99999 (99999 to 99999)	3.81 (1.77 to 7.39)
Other anogenital HPV associated cancers	99999 (99999 to 99999)	4.63 (1.94 to 14.29)	3.58 (2.04 to 7.49)	99999 (99999 to 99999)
SCCHN I-O naive	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cervical, Randomized	5.09 (1.87 to 9.07)	3.75 (3.32 to 9.23)	7.11 (3.71 to 17.25)	99999 (99999 to 99999)
Vaginal/Vulvar	3.75 (1.22 to 8.15)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
MCC	21.32 (9.20 to 62.52)	8.39 (3.71 to 24.34)	99999 (99999 to 99999)	99999 (99999 to 99999)
NPC	1.94 (1.54 to 3.58)	5.36 (2.37 to 9.23)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Metastatic Combo D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Months				
median (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)			
HPV positive SCCHN	99999 (99999 to 99999)			
Other anogenital HPV associated cancers	99999 (99999 to 99999)			
SCCHN I-O naive	1.81 (1.08 to 99999)			
Cervical, Randomized	99999 (99999 to 99999)			
Vaginal/Vulvar	99999 (99999 to 99999)			
MCC	99999 (99999 to 99999)			
NPC	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Metastatic: Investigator-Assessed Objective Response Rate (ORR) Extended Collection

End point title	Metastatic: Investigator-Assessed Objective Response Rate

	(ORR) Extended Collection[17]

End point description:

ORR is defined as the percentage of participants with a best overall response (BOR) of confirmed complete response (CR) or partial response (PR) using RECIST 1.1 criteria. An ORR in excess of 10% will be considered of clinical interest, and an ORR of 25% or greater will be considered of strong clinical interest.
Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Participants with the following diseases will be assessed:
1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)
Note: "Cervical, Randomized" and "Cervical, Pooled" are not mutually exclusive categories
99999=NA

End point type	Post-hoc

End point timeframe:

From the date of first dose to the date of the initial objectively documented tumor progression or the date of the last tumor assessment prior to subsequent therapy (Up to 83 months)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only specified arms planned for this endpoint

End point values	Metastatic Monotherapy	Metastatic Combo A	Metastatic Combo B	Metastatic Combo C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	195	133	8
Units: Percentage of participants				
number (confidence interval 95%)				
EBV positive related gastric cancer	14.3 (1.8 to 42.8)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
HPV positive SCCHN	11.5 (2.4 to 30.2)	31.0 (17.6 to 47.1)	99999 (99999 to 99999)	0 (0.0 to 36.9)
Other anogenital HPV associated cancers	99999 (99999 to 99999)	34.8 (16.4 to 57.3)	23.8 (8.2 to 47.2)	99999 (99999 to 99999)
SCCHN I-O naive	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cervical, Randomized	26.3 (9.1 to 51.2)	31.1 (18.2 to 46.6)	99999 (99999 to 99999)	99999 (99999 to 99999)
Cervical, Pooled	99999 (99999 to 99999)	99999 (99999 to 99999)	40.2 (31.0 to 49.9)	99999 (99999 to 99999)
Vaginal/Vulvar	20.0 (0.5 to 71.6)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
MCC	60.0 (38.7 to 78.9)	58.1 (42.1 to 73.0)	99999 (99999 to 99999)	99999 (99999 to 99999)
NPC	16.7 (4.7 to 37.4)	28.6 (15.7 to 44.6)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Metastatic Combo D			
Subject group type	Reporting group			
Number of subjects analysed	6			

Units: Percentage of participants				
number (confidence interval 95%)				
EBV positive related gastric cancer	99999 (99999 to 99999)			
HPV positive SCCHN	99999 (99999 to 99999)			
Other anogenital HPV associated cancers	99999 (99999 to 99999)			
SCCHN I-O naive	16.7 (0.4 to 64.1)			
Cervical, Randomized	99999 (99999 to 99999)			
Cervical, Pooled	99999 (99999 to 99999)			
Vaginal/Vulvar	99999 (99999 to 99999)			
MCC	99999 (99999 to 99999)			
NPC	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

SAEs and NSAEs are assessed from first dose to 100 days post last dose (Up to 83 months) Participants were assessed for deaths (all-causes) from their first dose to their study completion (Up to 84 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Metastatic Monotherapy

Reporting group description:

Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Reporting group title	Neoadjuvant

Reporting group description:

Nivolumab IV over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15

Reporting group title	Metastatic Combo D

Reporting group description:

Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Reporting group title	Metastatic Combo B

Reporting group description:

Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Reporting group title	Metastatic Combo C

Reporting group description:

Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Reporting group title	Metastatic Combo A

Reporting group description:

Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

Serious adverse events	Metastatic Monotherapy	Neoadjuvant	Metastatic Combo D
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 113 (52.21%)	40 / 123 (32.52%)	5 / 6 (83.33%)
number of deaths (all causes)	82	40	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	24 / 113 (21.24%)	2 / 123 (1.63%)	3 / 6 (50.00%)
occurrences causally related to treatment / all	0 / 26	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 19	0 / 2	0 / 3
Acute myeloid leukaemia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Infected neoplasm			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 melanoma			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Tumour obstruction			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Metastasis			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial haemorrhage			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac vein stenosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Debridement			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Chills			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Facial pain			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Disease progression			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Death			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Complication associated with device			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Mucosal inflammation			
subjects affected / exposed	0 / 113 (0.00%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Sudden death			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 113 (2.65%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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

Prostatic obstruction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval disorder			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 113 (0.00%)	2 / 123 (1.63%)	0 / 6 (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
Hypoxia			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Haemoptysis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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

Dyspnoea			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (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
Asthma			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stridor			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Pneumonitis			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Productive cough			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical condition abnormal			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 bilirubin increased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 magnesium decreased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 pressure decreased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus test positive			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 syncytial virus test positive			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Troponin increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urine output decreased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural fistula			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Transfusion reaction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Postoperative wound complication			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Procedural pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Recall phenomenon			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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 failure			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (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
Cardiac tamponade			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune pericarditis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Coronary artery disease			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Angina pectoris			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Cerebral ischaemia			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery aneurysm			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bell's palsy			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal ganglia infarction			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Headache			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Monoparesis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 113 (0.00%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anaemia			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Lymph node pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Constipation			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal disorder			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Gastritis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 113 (0.88%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossodynia			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Ileus			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Intestinal perforation			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Immune-mediated pancreatitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal motility disorder			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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 haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Pancreatitis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Proctalgia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (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
Stomatitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune cholangitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Biliary tract disorder			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 obstruction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder rupture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cytolysis			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pruritic			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Hydronephrosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (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
Oliguria			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urogenital fistula			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 incontinence			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haematoma			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid disorder			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Gastroenteritis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Clostridial sepsis			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site infection			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Post procedural infection			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 113 (2.65%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (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
Tuberculosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
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	3 / 113 (2.65%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (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
Dehydration			

subjects affected / exposed	1 / 113 (0.88%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (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
Hyperglycaemia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Metastatic Combo B	Metastatic Combo C	Metastatic Combo A
Total subjects affected by serious adverse events			
subjects affected / exposed	99 / 133 (74.44%)	5 / 8 (62.50%)	130 / 195 (66.67%)
number of deaths (all causes)	86	7	133
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	21 / 133 (15.79%)	2 / 8 (25.00%)	39 / 195 (20.00%)
occurrences causally related to treatment / all	0 / 21	0 / 2	0 / 40
deaths causally related to treatment / all	0 / 20	0 / 2	0 / 34
Acute myeloid leukaemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected neoplasm			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung adenocarcinoma			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma of the skin			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastasis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (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
Orthostatic hypotension			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac vein stenosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Debridement			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chills			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical health deterioration			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Death			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Complication associated with device			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	5 / 195 (2.56%)
occurrences causally related to treatment / all	3 / 9	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	0 / 195 (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
Prostatic obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (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
Female genital tract fistula			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspiration			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 133 (0.00%)	2 / 8 (25.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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 lung disease			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Pleural effusion			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stridor			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	10 / 133 (7.52%)	0 / 8 (0.00%)	7 / 195 (3.59%)
occurrences causally related to treatment / all	10 / 10	0 / 0	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Confusional state			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (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
Blood magnesium decreased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood pressure decreased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urine output decreased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			

subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural fistula			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Post procedural haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			

subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	0 / 195 (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
Recall phenomenon			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Spinal compression fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
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 disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac arrest			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Autoimmune pericarditis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
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			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocarditis			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Carotid artery aneurysm			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bell's palsy			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal ganglia infarction			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Guillain-Barre syndrome			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Embolic stroke			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
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 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intraventricular haemorrhage			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Peripheral motor neuropathy			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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			
Febrile neutropenia			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	5 / 133 (3.76%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	3 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node pain			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	11 / 133 (8.27%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	13 / 13	0 / 0	3 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal disorder			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences causally related to treatment / all	3 / 4	0 / 0	8 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Glossodynia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	0 / 195 (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
Immune-mediated enterocolitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intestinal obstruction			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated pancreatitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Oesophageal motility disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Proctalgia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Small intestinal obstruction			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (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
Stomatitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Hepatobiliary disorders			
Autoimmune cholangitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Cholecystitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Autoimmune hepatitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder rupture			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	6 / 133 (4.51%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cytolysis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Rash maculo-papular			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pruritic			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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 nephritis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Acute kidney injury			
subjects affected / exposed	8 / 133 (6.02%)	0 / 8 (0.00%)	5 / 195 (2.56%)
occurrences causally related to treatment / all	4 / 8	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urogenital fistula			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid disorder			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Hypothyroidism			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
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 neck			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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
Device related sepsis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
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 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial sepsis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (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
Meningitis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Large intestine infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
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 tract infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Septic shock			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Sinusitis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyponatraemia			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
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	1 / 133 (0.75%)	0 / 8 (0.00%)	0 / 195 (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

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

Non-serious adverse events	Metastatic Monotherapy	Neoadjuvant	Metastatic Combo D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 113 (97.35%)	108 / 123 (87.80%)	5 / 6 (83.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	7 / 113 (6.19%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 113 (2.65%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Vascular disorders			
Lymphoedema			
subjects affected / exposed	4 / 113 (3.54%)	2 / 123 (1.63%)	1 / 6 (16.67%)
occurrences (all)	4	2	1
Hypotension			

subjects affected / exposed	5 / 113 (4.42%)	4 / 123 (3.25%)	1 / 6 (16.67%)
occurrences (all)	5	4	1
Hypertension			
subjects affected / exposed	10 / 113 (8.85%)	12 / 123 (9.76%)	0 / 6 (0.00%)
occurrences (all)	13	12	0
Haematoma			
subjects affected / exposed	2 / 113 (1.77%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Venous thrombosis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Gait disturbance			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	47 / 113 (41.59%)	40 / 123 (32.52%)	1 / 6 (16.67%)
occurrences (all)	60	43	1
Facial pain			
subjects affected / exposed	3 / 113 (2.65%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	3	3	1
Face oedema			
subjects affected / exposed	2 / 113 (1.77%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	2	3	1
Chills			
subjects affected / exposed	6 / 113 (5.31%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	7	3	0
Chest pain			
subjects affected / exposed	6 / 113 (5.31%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Asthenia			

subjects affected / exposed	18 / 113 (15.93%)	11 / 123 (8.94%)	0 / 6 (0.00%)
occurrences (all)	26	11	0
Influenza like illness			
subjects affected / exposed	4 / 113 (3.54%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	4	3	0
Malaise			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Localised oedema			
subjects affected / exposed	0 / 113 (0.00%)	8 / 123 (6.50%)	0 / 6 (0.00%)
occurrences (all)	0	8	0
Mucosal inflammation			
subjects affected / exposed	4 / 113 (3.54%)	15 / 123 (12.20%)	0 / 6 (0.00%)
occurrences (all)	4	15	0
Non-cardiac chest pain			
subjects affected / exposed	5 / 113 (4.42%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences (all)	5	2	0
Pyrexia			
subjects affected / exposed	14 / 113 (12.39%)	13 / 123 (10.57%)	2 / 6 (33.33%)
occurrences (all)	17	15	2
Pain			
subjects affected / exposed	3 / 113 (2.65%)	2 / 123 (1.63%)	1 / 6 (16.67%)
occurrences (all)	3	2	1
Oedema peripheral			
subjects affected / exposed	16 / 113 (14.16%)	6 / 123 (4.88%)	2 / 6 (33.33%)
occurrences (all)	16	6	2
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	3	5	0
Pelvic pain			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			

Pneumonitis			
subjects affected / exposed	8 / 113 (7.08%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	9	0	0
Pleural effusion			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Oropharyngeal pain			
subjects affected / exposed	6 / 113 (5.31%)	6 / 123 (4.88%)	1 / 6 (16.67%)
occurrences (all)	6	8	1
Nasal congestion			
subjects affected / exposed	5 / 113 (4.42%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Laryngeal inflammation			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	7 / 113 (6.19%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Dyspnoea			
subjects affected / exposed	21 / 113 (18.58%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	25	3	1
Cough			
subjects affected / exposed	26 / 113 (23.01%)	7 / 123 (5.69%)	1 / 6 (16.67%)
occurrences (all)	33	8	1
Aspiration			
subjects affected / exposed	0 / 113 (0.00%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Productive cough			
subjects affected / exposed	3 / 113 (2.65%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			

subjects affected / exposed	10 / 113 (8.85%)	9 / 123 (7.32%)	0 / 6 (0.00%)
occurrences (all)	10	9	0
Confusional state			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	10 / 113 (8.85%)	2 / 123 (1.63%)	1 / 6 (16.67%)
occurrences (all)	12	2	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 113 (7.08%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	10	4	0
Amylase increased			
subjects affected / exposed	6 / 113 (5.31%)	7 / 123 (5.69%)	0 / 6 (0.00%)
occurrences (all)	7	7	0
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 113 (8.85%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	12	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 113 (4.42%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	5	3	0
Blood creatinine increased			
subjects affected / exposed	11 / 113 (9.73%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	14	4	0
Breath sounds abnormal			
subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	17 / 113 (15.04%)	7 / 123 (5.69%)	0 / 6 (0.00%)
occurrences (all)	30	7	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 113 (0.88%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Platelet count decreased			

subjects affected / exposed	0 / 113 (0.00%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Troponin increased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	10 / 113 (8.85%)	15 / 123 (12.20%)	0 / 6 (0.00%)
occurrences (all)	10	15	0
White blood cell count decreased			
subjects affected / exposed	2 / 113 (1.77%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	3 / 113 (2.65%)	9 / 123 (7.32%)	0 / 6 (0.00%)
occurrences (all)	3	10	0
Infusion related reaction			
subjects affected / exposed	5 / 113 (4.42%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	6	4	0
Fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Radiation skin injury			
subjects affected / exposed	1 / 113 (0.88%)	15 / 123 (12.20%)	0 / 6 (0.00%)
occurrences (all)	1	15	0
Fall			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 113 (1.77%)	8 / 123 (6.50%)	1 / 6 (16.67%)
occurrences (all)	2	8	1
Paraesthesia			

subjects affected / exposed	2 / 113 (1.77%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Headache			
subjects affected / exposed	13 / 113 (11.50%)	6 / 123 (4.88%)	2 / 6 (33.33%)
occurrences (all)	15	6	2
Dysgeusia			
subjects affected / exposed	7 / 113 (6.19%)	10 / 123 (8.13%)	0 / 6 (0.00%)
occurrences (all)	7	10	0
Dizziness			
subjects affected / exposed	12 / 113 (10.62%)	6 / 123 (4.88%)	0 / 6 (0.00%)
occurrences (all)	12	7	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 113 (24.78%)	11 / 123 (8.94%)	2 / 6 (33.33%)
occurrences (all)	32	12	4
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 113 (2.65%)	2 / 123 (1.63%)	1 / 6 (16.67%)
occurrences (all)	4	2	1
Vertigo			
subjects affected / exposed	6 / 113 (5.31%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	9	0	0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 113 (1.77%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	3	5	0
Abdominal pain upper			
subjects affected / exposed	12 / 113 (10.62%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	13	1	0
Constipation			
subjects affected / exposed	27 / 113 (23.89%)	21 / 123 (17.07%)	0 / 6 (0.00%)
occurrences (all)	31	21	0
Abdominal pain			
subjects affected / exposed	18 / 113 (15.93%)	8 / 123 (6.50%)	0 / 6 (0.00%)
occurrences (all)	20	8	0
Tongue ulceration			

subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	7 / 113 (6.19%)	5 / 123 (4.07%)	0 / 6 (0.00%)
occurrences (all)	7	5	0
Nausea			
subjects affected / exposed	25 / 113 (22.12%)	42 / 123 (34.15%)	3 / 6 (50.00%)
occurrences (all)	30	47	3
Dysphagia			
subjects affected / exposed	10 / 113 (8.85%)	21 / 123 (17.07%)	0 / 6 (0.00%)
occurrences (all)	10	21	0
Dyspepsia			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Dry mouth			
subjects affected / exposed	8 / 113 (7.08%)	6 / 123 (4.88%)	0 / 6 (0.00%)
occurrences (all)	8	6	0
Diarrhoea			
subjects affected / exposed	31 / 113 (27.43%)	22 / 123 (17.89%)	2 / 6 (33.33%)
occurrences (all)	54	23	2
Vomiting			
subjects affected / exposed	21 / 113 (18.58%)	14 / 123 (11.38%)	0 / 6 (0.00%)
occurrences (all)	29	17	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	17 / 113 (15.04%)	7 / 123 (5.69%)	0 / 6 (0.00%)
occurrences (all)	22	7	0
Pruritus			
subjects affected / exposed	23 / 113 (20.35%)	11 / 123 (8.94%)	1 / 6 (16.67%)
occurrences (all)	30	11	2
Night sweats			
subjects affected / exposed	1 / 113 (0.88%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	1	1	0

Dry skin			
subjects affected / exposed	10 / 113 (8.85%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	10	3	1
Rash maculo-papular			
subjects affected / exposed	8 / 113 (7.08%)	6 / 123 (4.88%)	0 / 6 (0.00%)
occurrences (all)	12	6	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 113 (1.77%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Hypothyroidism			
subjects affected / exposed	17 / 113 (15.04%)	3 / 123 (2.44%)	1 / 6 (16.67%)
occurrences (all)	17	3	1
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	2 / 113 (1.77%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Flank pain			
subjects affected / exposed	6 / 113 (5.31%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Back pain			
subjects affected / exposed	17 / 113 (15.04%)	4 / 123 (3.25%)	1 / 6 (16.67%)
occurrences (all)	20	4	1
Arthralgia			
subjects affected / exposed	24 / 113 (21.24%)	10 / 123 (8.13%)	1 / 6 (16.67%)
occurrences (all)	28	10	1
Muscular weakness			
subjects affected / exposed	2 / 113 (1.77%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Pain in extremity			
subjects affected / exposed	12 / 113 (10.62%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	12	4	0
Neck pain			
subjects affected / exposed	3 / 113 (2.65%)	6 / 123 (4.88%)	0 / 6 (0.00%)
occurrences (all)	4	6	0
Myalgia			

subjects affected / exposed	10 / 113 (8.85%)	6 / 123 (4.88%)	0 / 6 (0.00%)
occurrences (all)	10	6	0
Musculoskeletal pain			
subjects affected / exposed	4 / 113 (3.54%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Musculoskeletal chest pain			
subjects affected / exposed	8 / 113 (7.08%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	8	0	0
Infections and infestations			
Oral bacterial infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	10 / 113 (8.85%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	16	0	0
Mucosal infection			
subjects affected / exposed	2 / 113 (1.77%)	1 / 123 (0.81%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Eye infection			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	6 / 113 (5.31%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Candida infection			
subjects affected / exposed	3 / 113 (2.65%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Bronchitis			
subjects affected / exposed	8 / 113 (7.08%)	1 / 123 (0.81%)	0 / 6 (0.00%)
occurrences (all)	8	1	0
Otitis externa			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	9 / 113 (7.96%)	9 / 123 (7.32%)	0 / 6 (0.00%)
occurrences (all)	9	11	0

Upper respiratory tract infection			
subjects affected / exposed	7 / 113 (6.19%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	9	0	0
Tracheitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	6 / 113 (5.31%)	0 / 123 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Respiratory tract infection			
subjects affected / exposed	3 / 113 (2.65%)	0 / 123 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 113 (21.24%)	15 / 123 (12.20%)	1 / 6 (16.67%)
occurrences (all)	29	16	1
Hypophosphataemia			
subjects affected / exposed	5 / 113 (4.42%)	4 / 123 (3.25%)	0 / 6 (0.00%)
occurrences (all)	8	4	0
Hyponatraemia			
subjects affected / exposed	4 / 113 (3.54%)	9 / 123 (7.32%)	1 / 6 (16.67%)
occurrences (all)	4	9	1
Hypokalaemia			
subjects affected / exposed	6 / 113 (5.31%)	11 / 123 (8.94%)	0 / 6 (0.00%)
occurrences (all)	10	12	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 113 (1.77%)	2 / 123 (1.63%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Hyperglycaemia			
subjects affected / exposed	3 / 113 (2.65%)	3 / 123 (2.44%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Hypercalcaemia			
subjects affected / exposed	3 / 113 (2.65%)	2 / 123 (1.63%)	1 / 6 (16.67%)
occurrences (all)	5	3	1
Dehydration			

subjects affected / exposed	1 / 113 (0.88%)	8 / 123 (6.50%)	0 / 6 (0.00%)
occurrences (all)	1	9	0
Hypomagnesaemia			
subjects affected / exposed	10 / 113 (8.85%)	10 / 123 (8.13%)	0 / 6 (0.00%)
occurrences (all)	10	10	0

Non-serious adverse events	Metastatic Combo B	Metastatic Combo C	Metastatic Combo A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	129 / 133 (96.99%)	7 / 8 (87.50%)	189 / 195 (96.92%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 133 (2.26%)	1 / 8 (12.50%)	5 / 195 (2.56%)
occurrences (all)	3	1	5
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Vascular disorders			
Lymphoedema			
subjects affected / exposed	5 / 133 (3.76%)	1 / 8 (12.50%)	4 / 195 (2.05%)
occurrences (all)	5	1	4
Hypotension			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	10 / 195 (5.13%)
occurrences (all)	5	0	16
Hypertension			
subjects affected / exposed	5 / 133 (3.76%)	1 / 8 (12.50%)	7 / 195 (3.59%)
occurrences (all)	5	1	7
Haematoma			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	2 / 195 (1.03%)
occurrences (all)	0	1	2
Venous thrombosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0

Gait disturbance			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences (all)	1	0	2
Fatigue			
subjects affected / exposed	46 / 133 (34.59%)	6 / 8 (75.00%)	81 / 195 (41.54%)
occurrences (all)	53	6	85
Facial pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences (all)	1	0	7
Chills			
subjects affected / exposed	9 / 133 (6.77%)	0 / 8 (0.00%)	10 / 195 (5.13%)
occurrences (all)	11	0	11
Chest pain			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	2 / 195 (1.03%)
occurrences (all)	1	1	2
Asthenia			
subjects affected / exposed	23 / 133 (17.29%)	0 / 8 (0.00%)	26 / 195 (13.33%)
occurrences (all)	25	0	32
Influenza like illness			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	12 / 195 (6.15%)
occurrences (all)	2	0	14
Malaise			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	3 / 195 (1.54%)
occurrences (all)	0	1	3
Localised oedema			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences (all)	0	0	2
Mucosal inflammation			
subjects affected / exposed	5 / 133 (3.76%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences (all)	8	0	6
Non-cardiac chest pain			
subjects affected / exposed	3 / 133 (2.26%)	1 / 8 (12.50%)	3 / 195 (1.54%)
occurrences (all)	4	1	4

Pyrexia			
subjects affected / exposed	33 / 133 (24.81%)	0 / 8 (0.00%)	34 / 195 (17.44%)
occurrences (all)	43	0	37
Pain			
subjects affected / exposed	4 / 133 (3.01%)	1 / 8 (12.50%)	9 / 195 (4.62%)
occurrences (all)	4	1	9
Oedema peripheral			
subjects affected / exposed	20 / 133 (15.04%)	1 / 8 (12.50%)	21 / 195 (10.77%)
occurrences (all)	22	1	24
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences (all)	10	0	9
Pelvic pain			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences (all)	7	0	7
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	9 / 133 (6.77%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences (all)	10	0	12
Pleural effusion			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	4 / 195 (2.05%)
occurrences (all)	1	2	5
Oropharyngeal pain			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	10 / 195 (5.13%)
occurrences (all)	4	0	11
Nasal congestion			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences (all)	4	0	13
Laryngeal inflammation			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	1	0	4
Dyspnoea			

subjects affected / exposed	13 / 133 (9.77%)	2 / 8 (25.00%)	30 / 195 (15.38%)
occurrences (all)	16	2	34
Cough			
subjects affected / exposed	17 / 133 (12.78%)	2 / 8 (25.00%)	49 / 195 (25.13%)
occurrences (all)	21	3	64
Aspiration			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	0	0	4
Productive cough			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	7 / 195 (3.59%)
occurrences (all)	8	0	8
Upper-airway cough syndrome			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	6 / 195 (3.08%)
occurrences (all)	1	1	9
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 133 (3.01%)	1 / 8 (12.50%)	8 / 195 (4.10%)
occurrences (all)	4	1	9
Confusional state			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	5 / 195 (2.56%)
occurrences (all)	2	0	5
Insomnia			
subjects affected / exposed	8 / 133 (6.02%)	1 / 8 (12.50%)	23 / 195 (11.79%)
occurrences (all)	8	1	26
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	22 / 133 (16.54%)	0 / 8 (0.00%)	26 / 195 (13.33%)
occurrences (all)	30	0	31
Amylase increased			
subjects affected / exposed	12 / 133 (9.02%)	1 / 8 (12.50%)	20 / 195 (10.26%)
occurrences (all)	14	1	33
Aspartate aminotransferase increased			
subjects affected / exposed	20 / 133 (15.04%)	0 / 8 (0.00%)	25 / 195 (12.82%)
occurrences (all)	31	0	31
Blood alkaline phosphatase increased			

subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	10 / 195 (5.13%)
occurrences (all)	8	0	15
Blood creatinine increased			
subjects affected / exposed	13 / 133 (9.77%)	0 / 8 (0.00%)	19 / 195 (9.74%)
occurrences (all)	18	0	32
Breath sounds abnormal			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	2	0
Lipase increased			
subjects affected / exposed	17 / 133 (12.78%)	2 / 8 (25.00%)	27 / 195 (13.85%)
occurrences (all)	18	2	71
Lymphocyte count decreased			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	16 / 195 (8.21%)
occurrences (all)	3	0	20
Platelet count decreased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences (all)	0	0	18
Troponin increased			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	8 / 133 (6.02%)	2 / 8 (25.00%)	24 / 195 (12.31%)
occurrences (all)	8	2	28
White blood cell count decreased			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	10 / 195 (5.13%)
occurrences (all)	5	0	12
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences (all)	0	0	3
Infusion related reaction			

subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences (all)	5	0	16
Fracture			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Radiation skin injury			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	2 / 133 (1.50%)	1 / 8 (12.50%)	1 / 195 (0.51%)
occurrences (all)	2	1	1
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	4	0	6
Paraesthesia			
subjects affected / exposed	2 / 133 (1.50%)	2 / 8 (25.00%)	3 / 195 (1.54%)
occurrences (all)	2	2	3
Headache			
subjects affected / exposed	22 / 133 (16.54%)	0 / 8 (0.00%)	31 / 195 (15.90%)
occurrences (all)	32	0	41
Dysgeusia			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences (all)	3	0	3
Dizziness			
subjects affected / exposed	15 / 133 (11.28%)	0 / 8 (0.00%)	19 / 195 (9.74%)
occurrences (all)	19	0	22
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	42 / 133 (31.58%)	2 / 8 (25.00%)	53 / 195 (27.18%)
occurrences (all)	64	3	78
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	1	0	4
Vertigo			

subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	6 / 195 (3.08%)
occurrences (all)	8	0	7
Abdominal pain upper			
subjects affected / exposed	5 / 133 (3.76%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences (all)	5	0	9
Constipation			
subjects affected / exposed	37 / 133 (27.82%)	1 / 8 (12.50%)	51 / 195 (26.15%)
occurrences (all)	49	1	62
Abdominal pain			
subjects affected / exposed	30 / 133 (22.56%)	1 / 8 (12.50%)	28 / 195 (14.36%)
occurrences (all)	35	1	34
Tongue ulceration			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	1 / 195 (0.51%)
occurrences (all)	1	1	1
Stomatitis			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	5 / 195 (2.56%)
occurrences (all)	4	0	8
Nausea			
subjects affected / exposed	48 / 133 (36.09%)	2 / 8 (25.00%)	45 / 195 (23.08%)
occurrences (all)	75	2	55
Dysphagia			
subjects affected / exposed	2 / 133 (1.50%)	4 / 8 (50.00%)	12 / 195 (6.15%)
occurrences (all)	2	4	12
Dyspepsia			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences (all)	7	0	12
Dry mouth			
subjects affected / exposed	6 / 133 (4.51%)	1 / 8 (12.50%)	13 / 195 (6.67%)
occurrences (all)	6	1	15
Diarrhoea			
subjects affected / exposed	54 / 133 (40.60%)	1 / 8 (12.50%)	61 / 195 (31.28%)
occurrences (all)	91	4	108

Vomiting			
subjects affected / exposed	33 / 133 (24.81%)	1 / 8 (12.50%)	31 / 195 (15.90%)
occurrences (all)	49	1	38
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	2 / 195 (1.03%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	16 / 133 (12.03%)	1 / 8 (12.50%)	49 / 195 (25.13%)
occurrences (all)	24	1	65
Pruritus			
subjects affected / exposed	35 / 133 (26.32%)	0 / 8 (0.00%)	60 / 195 (30.77%)
occurrences (all)	40	0	77
Night sweats			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	3 / 195 (1.54%)
occurrences (all)	1	1	3
Dry skin			
subjects affected / exposed	12 / 133 (9.02%)	0 / 8 (0.00%)	14 / 195 (7.18%)
occurrences (all)	15	0	14
Rash maculo-papular			
subjects affected / exposed	25 / 133 (18.80%)	0 / 8 (0.00%)	20 / 195 (10.26%)
occurrences (all)	29	0	25
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	21 / 133 (15.79%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences (all)	24	0	9
Hypothyroidism			
subjects affected / exposed	31 / 133 (23.31%)	2 / 8 (25.00%)	39 / 195 (20.00%)
occurrences (all)	31	2	39
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	2 / 133 (1.50%)	1 / 8 (12.50%)	3 / 195 (1.54%)
occurrences (all)	2	1	3
Flank pain			
subjects affected / exposed	7 / 133 (5.26%)	0 / 8 (0.00%)	7 / 195 (3.59%)
occurrences (all)	8	0	7

Back pain			
subjects affected / exposed	19 / 133 (14.29%)	1 / 8 (12.50%)	28 / 195 (14.36%)
occurrences (all)	20	1	34
Arthralgia			
subjects affected / exposed	26 / 133 (19.55%)	2 / 8 (25.00%)	35 / 195 (17.95%)
occurrences (all)	29	2	44
Muscular weakness			
subjects affected / exposed	4 / 133 (3.01%)	1 / 8 (12.50%)	10 / 195 (5.13%)
occurrences (all)	7	1	10
Pain in extremity			
subjects affected / exposed	9 / 133 (6.77%)	0 / 8 (0.00%)	13 / 195 (6.67%)
occurrences (all)	9	0	14
Neck pain			
subjects affected / exposed	1 / 133 (0.75%)	1 / 8 (12.50%)	7 / 195 (3.59%)
occurrences (all)	1	1	8
Myalgia			
subjects affected / exposed	10 / 133 (7.52%)	0 / 8 (0.00%)	19 / 195 (9.74%)
occurrences (all)	10	0	21
Musculoskeletal pain			
subjects affected / exposed	2 / 133 (1.50%)	1 / 8 (12.50%)	5 / 195 (2.56%)
occurrences (all)	2	1	6
Musculoskeletal chest pain			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	11 / 195 (5.64%)
occurrences (all)	2	0	11
Infections and infestations			
Oral bacterial infection			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	14 / 195 (7.18%)
occurrences (all)	3	0	18
Mucosal infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	1 / 195 (0.51%)
occurrences (all)	0	0	1
Eye infection			

subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	3	0	4
Candida infection			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	5 / 195 (2.56%)
occurrences (all)	0	1	5
Bronchitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 8 (0.00%)	3 / 195 (1.54%)
occurrences (all)	2	0	3
Otitis externa			
subjects affected / exposed	0 / 133 (0.00%)	1 / 8 (12.50%)	0 / 195 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	31 / 133 (23.31%)	0 / 8 (0.00%)	21 / 195 (10.77%)
occurrences (all)	49	0	38
Upper respiratory tract infection			
subjects affected / exposed	8 / 133 (6.02%)	0 / 8 (0.00%)	27 / 195 (13.85%)
occurrences (all)	8	0	37
Tracheitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 8 (0.00%)	0 / 195 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	4 / 195 (2.05%)
occurrences (all)	5	0	4
Respiratory tract infection			
subjects affected / exposed	2 / 133 (1.50%)	0 / 8 (0.00%)	7 / 195 (3.59%)
occurrences (all)	2	0	7
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	32 / 133 (24.06%)	2 / 8 (25.00%)	48 / 195 (24.62%)
occurrences (all)	35	2	59
Hypophosphataemia			
subjects affected / exposed	3 / 133 (2.26%)	1 / 8 (12.50%)	20 / 195 (10.26%)
occurrences (all)	5	1	29

Hyponatraemia			
subjects affected / exposed	14 / 133 (10.53%)	1 / 8 (12.50%)	24 / 195 (12.31%)
occurrences (all)	20	1	38
Hypokalaemia			
subjects affected / exposed	15 / 133 (11.28%)	1 / 8 (12.50%)	20 / 195 (10.26%)
occurrences (all)	25	1	38
Hypoalbuminaemia			
subjects affected / exposed	16 / 133 (12.03%)	0 / 8 (0.00%)	14 / 195 (7.18%)
occurrences (all)	23	0	22
Hyperglycaemia			
subjects affected / exposed	9 / 133 (6.77%)	0 / 8 (0.00%)	16 / 195 (8.21%)
occurrences (all)	19	0	27
Hypercalcaemia			
subjects affected / exposed	4 / 133 (3.01%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences (all)	5	0	10
Dehydration			
subjects affected / exposed	3 / 133 (2.26%)	0 / 8 (0.00%)	9 / 195 (4.62%)
occurrences (all)	4	0	11
Hypomagnesaemia			
subjects affected / exposed	17 / 133 (12.78%)	1 / 8 (12.50%)	14 / 195 (7.18%)
occurrences (all)	27	1	32

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2015	inclusion criteria updated
16 October 2015	exclusion criteria update
16 March 2016	study design update
28 October 2016	study design and arm cohorts update
18 April 2018	enrollment and study design update
18 July 2018	enrollment and endpoints update
07 May 2019	endpoints update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported