



Clinical trial results:

A Phase 1/2 Study of the Combination of Lirilumab (Anti-KIR) Plus Nivolumab (Anti-PD-1) or Lirilumab Plus Nivolumab and Ipilimumab in Advanced Refractory Solid Tumors

Summary

EudraCT number	2016-001359-36
Trial protocol	IT FR ES
Global end of trial date	13 December 2019

Results information

Result version number	v1 (current)
This version publication date	24 December 2022
First version publication date	24 December 2022

Trial information

Trial identification

Sponsor protocol code	CA223-001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	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	26 August 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1: To assess the safety and tolerability of lirilumab given in combination with nivolumab and to identify DLTs and the MTD of the combination in subjects with advanced (metastatic and/or unresectable) solid tumors.

Part 2: To assess the safety and preliminary anti-tumor activity of the combination of lirilumab and nivolumab in subjects with advanced solid tumors.

Part 3: To estimate the ORR of lirilumab given in combination with nivolumab in subjects with recurrent or metastatic SCCHN that has relapsed or progressed within 6 months of the last dose of a platinum-containing therapy and whose tumors express PD-L1.

Part 5: To assess the safety and preliminary anti-tumor activity of the combination of lirilumab with nivolumab and ipilimumab in subjects with platinum-refractory recurrent or metastatic SCCHN.

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	12 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 105
Country: Number of subjects enrolled	United States: 190
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Switzerland: 1
Worldwide total number of subjects	337
EEA total number of subjects	146

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	215
From 65 to 84 years	121
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part 4 and Part 6 of the study were removed from the protocol study design prior to enrolling any subjects.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1/2 Liri 0.1 + Nivo 3

Arm description:

Participants receive Lirilumab 0.1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

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

Dosage and administration details:

3 mg/kg administered as a 60-minute infusion

Investigational medicinal product name	Lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

0.1 mg/kg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.

Arm title	Part 1/2: Liri 0.3 + Nivo 3
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Arm description:

Participants receive Lirilumab 0.3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

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

Dosage and administration details:

3 mg/kg administered as a 60-minute infusion

Investigational medicinal product name	Lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
0.3 mg/kg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Arm title	Part 1/2: Liri 1 + Nivo 3
Arm description:	
Participants receive Lirilumab 1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Arm type	Experimental
Investigational medicinal product name	Lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
1 mg/kg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	(BMS-936558
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
3 mg/kg administered as a 60-minute infusion	
Arm title	Part 1/2: Liri 3 + Nivo 3
Arm description:	
Participants receive Lirilumab 3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Arm type	Experimental
Investigational medicinal product name	Lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
3 mg/kg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	(BMS-936558
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
3 mg/kg administered as a 60-minute infusion	
Arm title	Part 3: PBO + Nivo 240
Arm description:	
Participants receive Placebo every 4 weeks (Q4W) and a flat dose of nivolumab monotherapy (240mg) every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Arm type	Experimental

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	BMS-936558
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
240 mg administered as a 30-minute infusion	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Normal Saline (ie, 0.9% Sodium Chloride Injection) administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Arm title	Part 3: Liri 240 + Nivo 240
Arm description:	
Participants receive Lirilumab 240 mg every 4 weeks (Q4W) and a flat dose of nivolumab 240 mg every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	BMS-936558
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
240 mg administered as a 30-minute infusion	
Investigational medicinal product name	lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
240 mg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Arm title	Part 5: Liri 3 + Nivo 3 + Ipi 1
Arm description:	
Participants receive Lirilumab 3 mg/kg IV every 4 weeks (Q4W), Nivolumab 3 mg/kg IV every 2 weeks (Q2W), and Ipilimumab 1 mg/kg IV every 6 weeks (Q6W) for 12-week cycles until progressive disease	
Arm type	Experimental
Investigational medicinal product name	lirilumab
Investigational medicinal product code	
Other name	BMS-986015
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
3 mg/kg administered as a 60-minute infusion, 30 minutes after completion of the nivolumab infusion.	
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	BMS-734016
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg administered as a 30-minute infusion, 30 minutes after completion of the nivolumab infusion.

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

Dosage and administration details:

3 mg/kg administered as a 30-minute infusion.

Number of subjects in period 1	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3
Started	4	16	15
Completed	0	6	5
Not completed	4	10	10
Adverse event, serious fatal	-	-	-
Disease progression	3	5	5
Participant withdrew consent	-	1	-
Poor/non-compliance	-	1	-
Study drug toxicity	1	1	1
Maximum clinical benefit	-	1	1
Adverse Event unrelated to drug	-	-	3
Other reason	-	-	-
No longer meets study criteria	-	-	-
Participant request to stop therapy	-	1	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Part 1/2: Liri 3 + Nivo 3	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240
Started	287	2	3
Completed	23	0	0
Not completed	264	2	3
Adverse event, serious fatal	1	-	-
Disease progression	204	1	3
Participant withdrew consent	8	-	-
Poor/non-compliance	1	-	-
Study drug toxicity	15	-	-
Maximum clinical benefit	3	-	-
Adverse Event unrelated to drug	21	-	-
Other reason	3	1	-
No longer meets study criteria	1	-	-
Participant request to stop therapy	6	-	-

Lost to follow-up	1	-	-
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Number of subjects in period 1	Part 5: Liri 3 + Nivo 3 + Ipi 1
Started	10
Completed	0
Not completed	10
Adverse event, serious fatal	-
Disease progression	5
Participant withdrew consent	-
Poor/non-compliance	-
Study drug toxicity	5
Maximum clinical benefit	-
Adverse Event unrelated to drug	-
Other reason	-
No longer meets study criteria	-
Participant request to stop therapy	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1/2 Liri 0.1 + Nivo 3
Reporting group description: Participants receive Lirilumab 0.1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 0.3 + Nivo 3
Reporting group description: Participants receive Lirilumab 0.3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 1 + Nivo 3
Reporting group description: Participants receive Lirilumab 1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 3 + Nivo 3
Reporting group description: Participants receive Lirilumab 3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 3: PBO + Nivo 240
Reporting group description: Participants receive Placebo every 4 weeks (Q4W) and a flat dose of nivolumab monotherapy (240mg) every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Reporting group title	Part 3: Liri 240 + Nivo 240
Reporting group description: Participants receive Lirilumab 240 mg every 4 weeks (Q4W) and a flat dose of nivolumab 240 mg every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Reporting group title	Part 5: Liri 3 + Nivo 3 + Ipi 1
Reporting group description: Participants receive Lirilumab 3 mg/kg IV every 4 weeks (Q4W), Nivolumab 3 mg/kg IV every 2 weeks (Q2W), and Ipilimumab 1 mg/kg IV every 6 weeks (Q6W) for 12-week cycles until progressive disease	

Reporting group values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3
Number of subjects	4	16	15
Age Categorical			
Age categorical			
Units: Participants			
< 65 years old	4	10	9
>= 65 years old	0	6	6
Age Continuous			
Units: Years			
arithmetic mean	53.3	58.1	58.7
standard deviation	± 12.09	± 13.11	± 16.85
Sex: Female, Male			
Units: Participants			
Female	2	5	7
Male	2	11	8
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	4	16	15

Black/African American	0	0	0
American Indian / Alaska Native	0	0	0
Asian	0	0	0
Other	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	15	15
Unknown or Not Reported	0	1	0

Reporting group values	Part 1/2: Liri 3 + Nivo 3	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240
Number of subjects	287	2	3
Age Categorical			
Age categorical			
Units: Participants			
< 65 years old	184	1	2
>= 65 years old	103	1	1
Age Continuous			
Units: Years			
arithmetic mean	59.7	65.5	55.3
standard deviation	± 11.37	± 10.61	± 21.08
Sex: Female, Male			
Units: Participants			
Female	80	1	1
Male	207	1	2
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	237	2	3
Black/African American	10	0	0
American Indian / Alaska Native	1	0	0
Asian	10	0	0
Other	29	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	6	0	0
Not Hispanic or Latino	175	1	1
Unknown or Not Reported	106	1	2

Reporting group values	Part 5: Liri 3 + Nivo 3 + Ipi 1	Total	
Number of subjects	10	337	
Age Categorical			
Age categorical			
Units: Participants			
< 65 years old	5	215	
>= 65 years old	5	122	
Age Continuous			
Units: Years			
arithmetic mean	67.1	-	
standard deviation	± 10.40	-	

Sex: Female, Male			
Units: Participants			
Female	1	97	
Male	9	240	
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	10	287	
Black/African American	0	10	
American Indian / Alaska Native	0	1	
Asian	0	10	
Other	0	29	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	6	
Not Hispanic or Latino	8	219	
Unknown or Not Reported	2	112	

End points

End points reporting groups

Reporting group title	Part 1/2 Liri 0.1 + Nivo 3
Reporting group description: Participants receive Lirilumab 0.1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 0.3 + Nivo 3
Reporting group description: Participants receive Lirilumab 0.3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 1 + Nivo 3
Reporting group description: Participants receive Lirilumab 1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 1/2: Liri 3 + Nivo 3
Reporting group description: Participants receive Lirilumab 3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.	
Reporting group title	Part 3: PBO + Nivo 240
Reporting group description: Participants receive Placebo every 4 weeks (Q4W) and a flat dose of nivolumab monotherapy (240mg) every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Reporting group title	Part 3: Liri 240 + Nivo 240
Reporting group description: Participants receive Lirilumab 240 mg every 4 weeks (Q4W) and a flat dose of nivolumab 240 mg every 2 weeks (Q2W) for 8-week cycles until progressive disease.	
Reporting group title	Part 5: Liri 3 + Nivo 3 + Ipi 1
Reporting group description: Participants receive Lirilumab 3 mg/kg IV every 4 weeks (Q4W), Nivolumab 3 mg/kg IV every 2 weeks (Q2W), and Ipilimumab 1 mg/kg IV every 6 weeks (Q6W) for 12-week cycles until progressive disease	

Primary: Number of Participants with Adverse Events (AEs) - Parts 1, 2 and 5

End point title	Number of Participants with Adverse Events (AEs) - Parts 1, 2 and 5 ^{[1][2]}
End point description: An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment.	
End point type	Primary
End point timeframe: From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics planned for this endpoint

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

Justification: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Participants	4	16	15	284

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Participants	10			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events (SAEs) - Parts 1, 2 and 5

End point title	Number of Participants with Serious Adverse Events (SAEs) - Parts 1, 2 and 5 ^{[3][4]}
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End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Primary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics planned for this endpoint

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

Justification: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Participants	1	8	9	205

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Participants	7			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs) Leading to Discontinuation - Parts 1, 2 and 5

End point title	Number of Participants with Adverse Events (AEs) Leading to Discontinuation - Parts 1, 2 and 5 ^[5] ^[6]
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End point description:

Number of participants that experienced an AE leading to discontinuation during the course of the study. An AE is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment.

End point type	Primary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

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 statistics 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Participants	1	1	4	49

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Participants	5			

Statistical analyses

No statistical analyses for this end point

Primary: The Number of Participant Deaths in the Study - Parts 1, 2 and 5

End point title	The Number of Participant Deaths in the Study - Parts 1, 2 and 5 ^[7] ^[8]
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End point description:

The number of participants who died during the course of the study.

End point type	Primary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

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 statistics 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Participants	2	7	5	219

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Participants	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Clinical Laboratory Test Abnormalities - Parts 1, 2 and 5

End point title	Number of Participants with Clinical Laboratory Test Abnormalities - Parts 1, 2 and 5 ^{[9][10]}
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End point description:

Number of participants that experienced a clinical laboratory test abnormality during the course of the study, including hematology and serum chemistry, and thyroid panel abnormalities. Abnormalities considered are those Grade 3-4 events with a ≥ 1 grade increase from baseline. Laboratory tests are graded using National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 where Grade 3 is severe, and Grade 4 is life threatening. 99999= N/A (0 participants with available laboratory test measurements) NOTE: The number of participants analyzed for each laboratory parameter may vary depending on the number of participants with available laboratory test measurements. Baseline is defined as the last non-missing measurement prior to the first dosing date and time.

End point type	Primary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics planned for this endpoint

[10] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Participants				
Absolute Neutrophil Count - Grade 3	0	0	0	2
Absolute Neutrophil Count - Grade 4	0	1	0	0
Alanine Amino Transferase (ALT) - Grade 3	0	0	1	0
Alanine Amino Transferase (ALT) - Grade 4	0	0	0	0
Albumin - Grade 3	0	0	0	1
Albumin - Grade 4	0	0	0	0
Alkaline Phosphatase (ALP) - Grade 3	0	1	0	6
Alkaline Phosphatase (ALP) - Grade 4	0	0	0	0
Amylase, Total - Grade 3	0	0	0	8
Amylase, Total - Grade 4	0	0	0	1
APTT - Grade 3	99999	0	0	0
APTT - Grade 4	99999	0	0	0
Aspartate Aminotransferase (AST) - Grade 3	0	1	0	4
Aspartate Aminotransferase (AST) - Grade 4	0	0	1	0
Bilirubin, Total - Grade 3	0	0	0	1
Bilirubin, Total - Grade 4	0	0	0	0
Calcium, Corrected - Grade 3	99999	99999	99999	0
Calcium, Corrected - Grade 4	99999	99999	99999	0
Calcium, Ionized - Grade 3	99999	0	99999	0
Calcium, Ionized - Grade 4	99999	0	99999	0
Calcium, Total - Grade 3	0	0	0	6
Calcium, Total - Grade 4	0	0	0	4
Creatine Kinase (CK) - Grade 3	99999	99999	99999	0
Creatine Kinase (CK) - Grade 4	99999	99999	99999	0
Creatinine - Grade 3	0	0	0	0
Creatinine - Grade 4	0	0	0	0
Fibrinogen - Grade 3	99999	99999	99999	0
Fibrinogen - Grade 4	99999	99999	99999	0
G-Glutamyl Transferase (GGT) - Grade 3	99999	99999	99999	0
G-Glutamyl Transferase (GGT) - Grade 4	99999	99999	99999	0
Glucose, Fasting Serum - Grade 3	99999	0	99999	1
Glucose, Fasting Serum - Grade 4	99999	0	99999	0
Glucose, Serum - Grade 3	99999	99999	0	0
Glucose, Serum - Grade 4	99999	99999	0	0
Hemoglobin - Grade 3	0	1	1	24
Hemoglobin - Grade 4	0	0	0	0
Leukocytes - Grade 3	0	1	0	3
Leukocytes - Grade 4	0	0	0	3

Lipase, Total (Colorimetric Assay) - Grade 3	0	2	2	18
Lipase, Total (Colorimetric Assay) - Grade 4	0	0	0	7
Lipase, Total (Turbidimetric Assay) - Grade 3	99999	99999	99999	0
Lipase, Total (Turbidimetric Assay) - Grade 4	99999	99999	99999	0
Lymphocytes (Absolute) - Grade 3	0	3	4	64
Lymphocytes (Absolute) - Grade 4	0	0	0	9
Magnesium, Serum - Grade 3	0	0	0	1
Magnesium, Serum - Grade 4	0	0	0	1
Neutrophils (Absolute) - Grade 3	0	0	0	2
Neutrophils (Absolute) - Grade 4	99999	1	0	0
pH, Arterial Blood - Grade 3	99999	99999	99999	0
pH, Arterial Blood - Grade 4	0	99999	99999	0
Phosphorus, Inorganic - Grade 3	0	0	3	10
Phosphorus, Inorganic - Grade 4	0	0	0	0
Platelet Count - Grade 3	0	0	0	0
Platelet Count - Grade 4	0	0	0	1
Potassium, Serum - Grade 3	0	0	0	6
Potassium, Serum - Grade 4	0	0	0	3
Sodium Serum - Grade 3	0	1	1	26
Sodium Serum - Grade 4	0	0	0	0

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Participants				
Absolute Neutrophil Count - Grade 3	0			
Absolute Neutrophil Count - Grade 4	0			
Alanine Amino Transferase (ALT) - Grade 3	0			
Alanine Amino Transferase (ALT) - Grade 4	0			
Albumin - Grade 3	0			
Albumin - Grade 4	0			
Alkaline Phosphatase (ALP) - Grade 3	0			
Alkaline Phosphatase (ALP) - Grade 4	0			
Amylase, Total - Grade 3	0			
Amylase, Total - Grade 4	0			
APTT - Grade 3	0			
APTT - Grade 4	0			
Aspartate Aminotransferase (AST) - Grade 3	0			
Aspartate Aminotransferase (AST) - Grade 4	0			
Bilirubin, Total - Grade 3	0			
Bilirubin, Total - Grade 4	0			
Calcium, Corrected - Grade 3	0			
Calcium, Corrected - Grade 4	0			

Calcium, Ionized - Grade 3	0			
Calcium, Ionized - Grade 4	0			
Calcium, Total - Grade 3	0			
Calcium, Total - Grade 4	0			
Creatine Kinase (CK) - Grade 3	0			
Creatine Kinase (CK) - Grade 4	0			
Creatinine - Grade 3	1			
Creatinine - Grade 4	0			
Fibrinogen - Grade 3	0			
Fibrinogen - Grade 4	0			
G-Glutamyl Transferase (GGT) - Grade 3	99999			
G-Glutamyl Transferase (GGT) - Grade 4	99999			
Glucose, Fasting Serum - Grade 3	0			
Glucose, Fasting Serum - Grade 4	0			
Glucose, Serum - Grade 3	99999			
Glucose, Serum - Grade 4	99999			
Hemoglobin - Grade 3	1			
Hemoglobin - Grade 4	0			
Leukocytes - Grade 3	0			
Leukocytes - Grade 4	0			
Lipase, Total (Colorimetric Assay) - Grade 3	0			
Lipase, Total (Colorimetric Assay) - Grade 4	0			
Lipase, Total (Turbidimetric Assay) - Grade 3	99999			
Lipase, Total (Turbidimetric Assay) - Grade 4	99999			
Lymphocytes (Absolute) - Grade 3	4			
Lymphocytes (Absolute) - Grade 4	0			
Magnesium, Serum - Grade 3	0			
Magnesium, Serum - Grade 4	0			
Neutrophils (Absolute) - Grade 3	0			
Neutrophils (Absolute) - Grade 4	0			
pH, Arterial Blood - Grade 3	99999			
pH, Arterial Blood - Grade 4	99999			
Phosphorus, Inorganic - Grade 3	1			
Phosphorus, Inorganic - Grade 4	0			
Platelet Count - Grade 3	0			
Platelet Count - Grade 4	0			
Potassium, Serum - Grade 3	0			
Potassium, Serum - Grade 4	1			
Sodium Serum - Grade 3	1			
Sodium Serum - Grade 4	0			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR) ^[11]
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End point description:

Objective Response Rate (ORR) is defined as the percent of participants whose best overall response (BOR) is either a complete response (CR) or partial response (PR). BOR for a participant was derived using investigator-provided tumor measurements per RECIST v1.1. CR is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Primary
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End point timeframe:

From first dose up to approximately 2.5 years

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics planned for this endpoint

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	16	15	287
Units: Percentage of participants				
number (confidence interval 95%)	25.0 (0.6 to 80.6)	37.5 (15.2 to 64.6)	40.0 (16.3 to 67.7)	14.6 (10.8 to 19.3)

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240	Part 5: Liri 3 + Nivo 3 + Ipi 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	10	
Units: Percentage of participants				
number (confidence interval 95%)	50.0 (1.3 to 98.7)	0 (0.0 to 70.8)	0 (0.0 to 30.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) - Part 3

End point title	Disease Control Rate (DCR) - Part 3 ^[12]
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End point description:

Disease Control Rate (DCR) is defined as the percentage of participants with a best overall response (BOR) of complete response (CR), partial response (PR), or stable disease (SD). CR is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study. All participants will be monitored by radiographic assessment every 8 weeks from first dose to Week 48, and every 12 weeks thereafter until PD or treatment discontinuation.

End point type	Secondary
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End point timeframe:

From first dose up to approximately 2.5 years

Notes:

[12] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Percentage of participants				
number (confidence interval 95%)	50.0 (1.3 to 98.7)	33.3 (0.8 to 90.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Duration of Response (mDOR) - Parts 3 and 5

End point title	Median Duration of Response (mDOR) - Parts 3 and 5 ^[13]
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End point description:

DOR is defined as the time from the date of first response (CR or PR) to the date of first objectively documented tumor progression as determined using RECIST v1.1 or death due to any cause, whichever occurs first. Participant who remain alive and have not progressed were censored on the date of their last evaluable tumor assessment. Participants who started subsequent anticancer therapy without a prior reported progression were censored at the last evaluable tumor assessment prior to initiation of the subsequent anticancer therapy. CR is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. 99999 = N/A (Insufficient number of participants with events)

End point type	Secondary
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End point timeframe:

From first dose to the date of the first documented tumor progression as determined or death due to any cause, whichever occurs first. (Up to approximately 2.5 years)

Notes:

[13] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240	Part 5: Liri 3 + Nivo 3 + Ipi 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0 ^[14]	0 ^[15]	
Units: weeks				
median (full range (min-max))	99999 (40.0 to 99999)	(to)	(to)	

Notes:

[14] - 0 participants with a confirmed BOR of CR or PR.

[15] - 0 participants with a confirmed BOR of CR or PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Response (mTTR) - Part 3

End point title	Median Time to Response (mTTR) - Part 3 ^[16]
End point description: TTR is defined as the time from the first dosing date to the date of the first documented objective response (CR or PR). CR is defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.	
End point type	Secondary
End point timeframe: From date of first dose of study medication to the date of the first documented objective response (up to approximately 2.5 years)	
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: Endpoint is specific only to certain arms of the study	

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[17]		
Units: Weeks				
median (full range (min-max))	8.10 (8.1 to 8.1)	(to)		

Notes:
[17] - 0 participants with CR or PR

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with >=50% or >=80% Tumor Reduction - Parts 3 and 5

End point title	The Number of Participants with $\geq 50\%$ or $\geq 80\%$ Tumor Reduction - Parts 3 and 5 ^[18]
End point description: Depth of response is defined as the target tumor burden percent change from baseline at nadir for each participant as measured by the number of participants with $\geq 50\%$ and $\geq 80\%$ tumor reduction. Tumor assessments are performed every 8 weeks from first dose date for 48 weeks, and then every 12 weeks thereafter until progressive disease (PD) or treatment discontinuation, whichever occurs earlier.	
End point type	Secondary
End point timeframe: From first dose until progressive disease (PD) or treatment discontinuation, whichever occurs earlier. (Up to approximately 2.5 years)	
Notes: [18] - 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: Endpoint is specific only to certain arms of the study	

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240	Part 5: Liri 3 + Nivo 3 + Ipi 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	10	
Units: Participants				
WITH $\geq 50\%$ TUMOR REDUCTION	1	2	0	
WITH $\geq 80\%$ TUMOR REDUCTION	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) - Part 3

End point title	Overall Survival (OS) - Part 3 ^[19]
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End point description:

Overall Survival (OS) is defined as the time from date of first dose of study medication to the date of death for any cause. A subject who has not died will be censored at last known date alive. OS for a subject who initiated new cancer treatment, will also be censored at the date of the new treatment initiation. Estimated by Kaplan-Meier Method. 0.99999 = N/A (=Time point at which % of survivors drops below 50% has not been reached due to insufficient number of events and/or follow up)

End point type	Secondary
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End point timeframe:

From date of first dose of study medication to the date of death for any cause. (Up to approximately 2.5 years)

Notes:

[19] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Years				
median (full range (min-max))	0.99999 (0.2 to 1.2)	0.3 (0.1 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) - Part 3

End point title	Progression Free Survival (PFS) - Part 3 ^[20]
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End point description:

PFS is the time from the first dose to the date of first objectively documented disease progression or death due to any cause. Participants who died without a reported prior progression was considered to have progressed on the date of their death. Participants with no progression were censored on the last evaluable tumor assessment date. Participants who started subsequent therapy with no prior progression were censored at the last evaluable tumor assessment prior to initiation of the subsequent therapy. Participants with no post-baseline tumor assessment were censored on the date of first dose.

Progression is defined as at least a 20% increase in the sum of diameters of target lesions. The sum must also demonstrate an absolute increase of at least 5 mm (The appearance of new lesions is also considered progression and clinical deterioration in the absence of radiographic evidence is not).
9.99999 = N/A (Insufficient number of participants with events)

End point type	Secondary
End point timeframe:	
From first dose to the date of first objectively documented disease progression or death due to any cause, whichever occurs first. (Up to approximately 2.5 years)	

Notes:

[20] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Months				
median (full range (min-max))	9.99999 (1.1 to 11.0)	1.6 (1.1 to 7.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival Rate (PFSR) at 6 months - Part 3

End point title	Progression Free Survival Rate (PFSR) at 6 months - Part 3 ^[21]
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End point description:

Percentage of treated participants remaining progression free and surviving at 6 months. For those participants who remain alive and have not progressed, PFS will be censored on the date of the last tumor assessment. Progression is defined as At least a 20% increase in the sum of diameters of target lesions. The sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression). Clinical deterioration in the absence of radiographic evidence is not considered progression.

End point type	Secondary
End point timeframe:	
At 6 months after first dose	

Notes:

[21] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Percentage of participants				
number (confidence interval 95%)	50.0 (0.6 to 91.0)	33.3 (0.9 to 77.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) - Part 3

End point title	Number of Participants with Adverse Events (AEs) - Part 3 ^[22]
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End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment.

End point type	Secondary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[22] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serious Adverse Events (SAEs) - Part 3

End point title	Number of Participants with Serious Adverse Events (SAEs) - Part 3 ^[23]
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End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Secondary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[23] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) Leading to Discontinuation - Part 3

End point title	Number of Participants with Adverse Events (AEs) Leading to Discontinuation - Part 3 ^[24]
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End point description:

Number of participants that experienced an AE leading to discontinuation during the course of the study. An AE is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation subject administered an investigational (medicinal) product and that does not necessarily have a causal relationship with this treatment.

End point type	Secondary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[24] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participant Deaths in the Study - Part 3

End point title	The Number of Participant Deaths in the Study - Part 3 ^[25]
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End point description:

The number of participants who died during the course of the study.

End point type	Secondary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[25] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical Laboratory Test Abnormalities - Part 3

End point title	Number of Participants with Clinical Laboratory Test Abnormalities - Part 3 ^[26]
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End point description:

Number of participants that experienced a clinical laboratory test abnormality during the course of the study, including hematology and serum chemistry, and thyroid panel abnormalities. Abnormalities considered are those Grade 3-4 events with a ≥ 1 grade increase from baseline. Laboratory tests are graded using National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 where Grade 3 is severe, and Grade 4 is life threatening. 99999= N/A (0 participants with available laboratory test measurements) NOTE: The number of participants analyzed for each laboratory parameter may vary depending on the number of participants with available laboratory test measurements. Baseline is defined as the last non-missing measurement prior to the first dosing date and time.

End point type	Secondary
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End point timeframe:

From first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years)

Notes:

[26] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Participants				
Absolute Neutrophil Count - Grade 3	0	0		
Absolute Neutrophil Count - Grade 4	0	0		
Alanine Amino Transferase (ALT) - Grade 3	0	0		
Alanine Amino Transferase (ALT) - Grade 4	0	0		
Albumin - Grade 3	0	0		
Albumin - Grade 4	0	0		
Alkaline Phosphatase (ALP) - Grade 3	0	0		
Alkaline Phosphatase (ALP) - Grade 4	0	0		
Amylase, Total - Grade 3	1	0		
Amylase, Total - Grade 4	0	0		
APTT - Grade 3	99999	99999		
APTT - Grade 4	99999	99999		
Aspartate Aminotransferase (AST) - Grade 3	0	0		

Aspartate Aminotransferase (AST) - Grade 4	0	0		
Bilirubin, Total - Grade 3	0	0		
Bilirubin, Total - Grade 4	0	0		
Calcium, Corrected - Grade 3	99999	0		
Calcium, Corrected - Grade 4	99999	0		
Calcium, Ionized - Grade 3	0	99999		
Calcium, Ionized - Grade 4	0	99999		
Calcium, Total - Grade 3	0	0		
Calcium, Total - Grade 4	0	0		
Creatine Kinase (CK) - Grade 3	99999	99999		
Creatine Kinase (CK) - Grade 4	99999	99999		
Creatinine - Grade 3	0	0		
Creatinine - Grade 4	0	0		
Fibrinogen - Grade 3	99999	99999		
Fibrinogen - Grade 4	99999	99999		
G-Glutamyl Transferase (GGT) - Grade 3	0	0		
G-Glutamyl Transferase (GGT) - Grade 4	99999	99999		
Glucose, Fasting Serum - Grade 3	99999	99999		
Glucose, Fasting Serum - Grade 4	0	0		
Glucose, Serum - Grade 3	0	0		
Glucose, Serum - Grade 4	0	0		
Hemoglobin - Grade 3	0	0		
Hemoglobin - Grade 4	0	0		
Leukocytes - Grade 3	0	0		
Leukocytes - Grade 4	0	0		
Lipase, Total (Colorimetric Assay) - Grade 3	0	0		
Lipase, Total (Colorimetric Assay) - Grade 4	1	0		
Lipase, Total (Turbidimetric Assay) - Grade 3	99999	99999		
Lipase, Total (Turbidimetric Assay) - Grade 4	99999	99999		
Lymphocytes (Absolute) - Grade 3	0	2		
Lymphocytes (Absolute) - Grade 4	1	0		
Magnesium, Serum - Grade 3	0	0		
Magnesium, Serum - Grade 4	0	0		
Neutrophils (Absolute) - Grade 3	0	0		
Neutrophils (Absolute) - Grade 4	0	0		
pH, Arterial Blood - Grade 3	99999	99999		
pH, Arterial Blood - Grade 4	99999	99999		
Phosphorus, Inorganic - Grade 3	0	0		
Phosphorus, Inorganic - Grade 4	0	0		
Platelet Count - Grade 3	0	0		
Platelet Count - Grade 4	0	0		
Potassium, Serum - Grade 3	0	0		
Potassium, Serum - Grade 4	0	0		
Sodium Serum - Grade 3	0	0		
Sodium Serum - Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Drug Antibodies (ADA) - Parts 1, 2 and 5

End point title	Number of Participants with Anti-Drug Antibodies (ADA) - Parts 1, 2 and 5 ^[27]
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End point description:

Number of participants observed as ADA positive at baseline, ADA positive (post-baseline), and ADA negative (post-baseline). Baseline is defined as the last sample before initiation of treatment. Baseline ADA Positive Participant: A participant with baseline ADA positive sample. ADA Positive Participant: Participant with ≥ 1 ADA +ve sample relative to baseline (baseline ADA -ve, or ADA titer ≥ 9 -fold for Lirilumab and ≥ 4 -fold for Nivolumab relative to baseline +ve titer) at any time after first dose during the defined observation time period. ADA Negative Participant: A participant with no ADA positive sample after the initiation of treatment. 99999= N/A (0 participants who received at least 1 dose of drug and have at least 1 ADA sample available) NOTE: The number of participants analyzed for each ADA parameter may vary depending on the number of participants with available ADA samples.

End point type	Secondary
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End point timeframe:

From first dose to 100 days after last dose (up to approximately 126 weeks)

Notes:

[27] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	13	255
Units: Participants				
Baseline ADA Positive - Liri	0	2	0	21
ADA Positive - Liri	1	1	0	20
ADA Negative - Liri	3	10	10	234
Baseline ADA Positive - Nivo	0	1	3	14
ADA Positive - Nivo	0	1	0	43
ADA Negative - Nivo	4	14	13	212
Baseline ADA Positive - Ipi	99999	99999	99999	99999
ADA Positive - Ipi	99999	99999	99999	99999
ADA Negative - Ipi	99999	99999	99999	99999

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	4 ^[28]			

Units: Participants				
Baseline ADA Positive - Liri	1			
ADA Positive - Liri	0			
ADA Negative - Liri	4			
Baseline ADA Positive - Nivo	1			
ADA Positive - Nivo	0			
ADA Negative - Nivo	3			
Baseline ADA Positive - Ipi	1			
ADA Positive - Ipi	0			
ADA Negative - Ipi	3			

Notes:

[28] - 0 participants who received at least 1 dose of drug and have at least 1 ADA sample available

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with PD-L1 Status at Pretreatment - Parts 1, 2 and 5

End point title	The Number of Participants with PD-L1 Status at Pretreatment - Parts 1, 2 and 5 ^[29]
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End point description:

The number of participants with 1% or 5% PD-L1 expression in the tumor cell membrane. Participants are considered positive if they show $\geq 1\%$ or $\geq 5\%$ PD-L1 expression in the tumor cell membrane and negative if they show $< 1\%$ or $< 5\%$. PD-L1 expression is defined as the percent of tumor cells demonstrating plasma membrane PDL1 staining of any intensity. PD-L1 will be evaluated by immunohistochemistry (IHC). PD-L1 status at pretreatment is considered positive if any pretreatment sample is positive. PDL1= programmed cell death ligand 1

End point type	Secondary
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End point timeframe:

Pre-dose Day 1 (Cycles 1 ,3 ,5, 7, 9), Pre-dose Day 29 (Cycle 1, 2)

Notes:

[29] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	11	13	231
Units: Number of participants				
PD-L1 1 percent - positive	2	5	9	127
PD-L1 1 percent - negative	1	6	4	104
PD-L1 5 percent - positive	2	4	4	77
PD-L1 5 percent - negative	1	7	9	154

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Number of participants				

PD-L1 1 percent - positive	1			
PD-L1 1 percent - negative	0			
PD-L1 5 percent - positive	0			
PD-L1 5 percent - negative	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) - Parts 1, 2 and 5

End point title	Maximum Observed Plasma Concentration (Cmax) - Parts 1, 2 and 5 ^[30]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[30] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	13	11	249
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	2223.10 (± 27)	6509.35 (± 27)	22250.96 (± 29)	52034.18 (± 33)
Cycle 2	2277.39 (± 6)	7286.95 (± 24)	25623.89 (± 20)	69224.70 (± 26)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	65333.91 (± 3)			
Cycle 2	81600.00 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve from Time Zero to the Time of the Last Quantifiable Concentration [AUC(0-T)] - Parts 1, 2 and 5

End point title	Area Under the Plasma Concentration-Time Curve from Time Zero to the Time of the Last Quantifiable Concentration [AUC(0-T)] - Parts 1, 2 and 5 ^[31]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[31] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	13	11	249
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	360903.09 (± 23)	734836.53 (± 45)	4462883.03 (± 35)	9647500.52 (± 37)
Cycle 2	569516.79 (± 26)	1367259.80 (± 67)	6547184.03 (± 37)	11731186.91 (± 51)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	8819119.61 (± 29)			

Cycle 2	9958714.89 (\pm 99999)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval [AUC(TAU)] - Parts 1, 2 and 5

End point title	Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval [AUC(TAU)] - Parts 1, 2 and 5 ^[32]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[32] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	11	209
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	366418.73 (\pm 21)	1155363.50 (\pm 33)	4462883.03 (\pm 35)	11418017.10 (\pm 28)
Cycle 2	569516.79 (\pm 26)	1726615.52 (\pm 44)	6712959.58 (\pm 31)	18504162.18 (\pm 28)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	10843715.48 (\pm 99999)			
Cycle 2	99999 (\pm 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Observed Concentration (Tmax) - Parts 1, 2 and 5

End point title	Time of Maximum Observed Concentration (Tmax) - Parts 1, 2 and 5 ^[33]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data.

NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[33] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	13	11	249
Units: hour				
median (full range (min-max))				
Cycle 1	1.13 (1.0 to 1.3)	1.05 (0.8 to 21.7)	1.07 (1.0 to 1.6)	1.22 (0.1 to 161.3)
Cycle 2	1.08 (1.0 to 1.5)	1.02 (1.0 to 1.6)	1.13 (0.9 to 25.5)	1.18 (0.8 to 168.1)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hour				
median (full range (min-max))				
Cycle 1	1.03 (1.0 to 1.1)			
Cycle 2	1.33 (1.33 to 1.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (T-HALF) - Parts 1, 2 and 5

End point title Half-life (T-HALF) - Parts 1, 2 and 5^[34]

End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data.

End point type Secondary

End point timeframe:

Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[34] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	7	7	94
Units: hour				
arithmetic mean (standard deviation)	383.96 (± 235.421)	273.89 (± 234.588)	515.07 (± 361.525)	281.31 (± 237.236)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[35]			
Units: hour				
arithmetic mean (standard deviation)	()			

Notes:

[35] - 0 treated participants with available serum concentration data.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance per Time (CLT) - Parts 1, 2 and 5

End point title Clearance per Time (CLT) - Parts 1, 2 and 5^[36]

End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

End point type Secondary

End point timeframe:

Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[36] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	10	75
Units: liter per hour				
geometric mean (geometric coefficient of variation)	0.01 (± 22)	0.01 (± 38)	0.01 (± 35)	0.01 (± 30)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[37]			
Units: liter per hour				
geometric mean (geometric coefficient of variation)	()			

Notes:

[37] - 0 treated participants with available serum concentration data.

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Observed Concentration (Cmin, also known as CTAU) - Parts 1, 2 and 5

End point title	Trough Observed Concentration (Cmin, also known as CTAU) - Parts 1, 2 and 5 ^[38]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate)

NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[38] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	12	11	209
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	87.62 (± 77)	521.28 (± 60)	2572.90 (± 47)	6195.04 (± 45)
Cycle 2	358.55 (± 68)	1180.39 (± 65)	4827.27 (± 32)	11392.89 (± 45)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	5190.00 (± 99999)			
Cycle 2	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Pasma Concentration-Time Curve from Time Zero Extrapolated to Infinite Time ([AUC(INF)] - Parts 1, 2 and 5

End point title	Area Under the Pasma Concentration-Time Curve from Time Zero Extrapolated to Infinite Time ([AUC(INF)] - Parts 1, 2 and 5 ^[39]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data.

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[39] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[40]	0 ^[41]	0 ^[42]	0 ^[43]
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	()	()	()	()
Cycle 2	()	()	()	()

Notes:

[40] - 0 treated participants with available serum concentration data.

[41] - 0 treated participants with available serum concentration data.

[42] - 0 treated participants with available serum concentration data.

[43] - 0 treated participants with available serum concentration data.

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
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Subject group type	Reporting group			
Number of subjects analysed	0 ^[44]			
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	()			
Cycle 2	()			

Notes:

[44] - 0 treated participants with available serum concentration data.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution During Terminal Phase (V_z) - Parts 1, 2 and 5

End point title	Apparent Volume of Distribution During Terminal Phase (V _z) - Parts 1, 2 and 5 ^[45]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Based on the PK sample collections, PK parameters depended on terminal phase time points including AUC(INF) and V_z are not reportable

End point type	Secondary
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End point timeframe:

Pre-dose, end of infusion, 24, 168, and 336 hours post dose on day 1 cycle 1 and pre-dose on day 29 cycle 1. Pre-dose, end of infusion, 24 and 168 hours post dose on cycle 2 day 29.

Notes:

[45] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[46]	0 ^[47]	0 ^[48]	0 ^[49]
Units: liter				
geometric mean (geometric coefficient of variation)				
Cycle 1	()	()	()	()
Cycle 2	()	()	()	()

Notes:

[46] - 0 treated participants with available serum concentration data.

[47] - 0 treated participants with available serum concentration data.

[48] - 0 treated participants with available serum concentration data.

[49] - 0 treated participants with available serum concentration data.

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[50]			
Units: liter				
geometric mean (geometric coefficient of variation)				
Cycle 1	()			

Cycle 2	()			
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Notes:

[50] - 0 treated participants with available serum concentration data.

Statistical analyses

No statistical analyses for this end point

Secondary: End of Infusion Concentration (Ceoi) - Parts 1, 2 and 5 (Liri)

End point title	End of Infusion Concentration (Ceoi) - Parts 1, 2 and 5 (Liri) ^[51]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose and end of infusion on cycle 1 day 1 and cycle 2 day 29.

Notes:

[51] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	13	11	249
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	2223.10 (± 27)	6434.65 (± 28)	22250.96 (± 29)	45163.87 (± 38)
Cycle 2 Day 29	2277.39 (± 6)	7286.95 (± 24)	25185.06 (± 20)	65874.20 (± 30)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	65333.91 (± 3)			
Cycle 2 Day 29	81600.00 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough - Parts 1, 2 and 5 (Liri)

End point title	Ctrough - Parts 1, 2 and 5 (Liri) ^[52]
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End point description:

Pharmacokinetics of lirilumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose on cycle 1 day 29 and Pre-dose and end of infusion on cycle 2 day 29.

Notes:

[52] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	12	11	200
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 29	192.29 (± 42)	521.28 (± 60)	2572.90 (± 47)	6195.08 (± 45)
Cycle 2 Day 29	327.50 (± 85)	1069.84 (± 63)	4592.95 (± 32)	10865.91 (± 45)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 29	5190.00 (± 99999)			
Cycle 2 Day 29	19100.00 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: End of Infusion Concentration (Ceoi) - Parts 1, 2 and 5 (Nivo)

End point title	End of Infusion Concentration (Ceoi) - Parts 1, 2 and 5
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End point description:

Pharmacokinetics of nivolumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

99999= N/A (insufficient number of participants with available serum concentration data to calculate %CV) NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

Pre-dose and end of infusion on cycle 1 day 1 and cycle 2 day 29.

Notes:

[53] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	15	11	253
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	63.16 (± 31)	66.33 (± 16)	66.16 (± 24)	52.48 (± 25)
Cycle 2 Day 29	104.47 (± 16)	114.89 (± 28)	116.08 (± 17)	99.75 (± 25)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	44.75 (± 15)			
Cycle 2 Day 29	115.37 (± 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough - Parts 1, 2 and 5 (Nivo)

End point title	Ctrough - Parts 1, 2 and 5 (Nivo) ^[54]
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End point description:

Pharmacokinetics of nivolumab were derived from serum concentration versus time data. Geometric CV data is not available, therefore the Arithmetic %CV is represented in the table below.

NOTE: The number of participants analyzed for each cycle may vary depending on the number of participants with available serum concentration data.

End point type	Secondary
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End point timeframe:

336 hours post dose on cycle 1 day 1 (cycle 1 day 15) and pre-dose and end of infusion on cycle 2 day 29.

Notes:

[54] - 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: Endpoint is specific only to certain arms of the study

End point values	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3	Part 1/2: Liri 3 + Nivo 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	14	15	244
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15	19.15 (± 16)	20.14 (± 24)	21.36 (± 24)	15.81 (± 32)
Cycle 2 Day 29	55.67 (± 42)	62.18 (± 38)	71.31 (± 21)	50.07 (± 32)

End point values	Part 5: Liri 3 + Nivo 3 + Ipi 1			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15	17.30 (± 19)			
Cycle 2 Day 29	62.62 (± 17)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality was assessed from first dose to study completion (up to 2.5 years). SAEs and NAEs were assessed from first dose to 150 days post last dose (up to an average of 51 weeks and a maximum of 2.5 years).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Part 1/2 Liri 0.1 + Nivo 3
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Reporting group description:

Participants receive Lirilumab 0.1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

Reporting group title	Part 1/2: Liri 0.3 + Nivo 3
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Reporting group description:

Participants receive Lirilumab 0.3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

Reporting group title	Part 1/2: Liri 1 + Nivo 3
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Reporting group description:

Participants receive Lirilumab 1 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

Reporting group title	Part 1/2: Liri 3 + Nivo 3
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Reporting group description:

Participants receive Lirilumab 3 mg/kg every 4 weeks (Q4W) and Nivolumab 3 mg/kg every 2 weeks (Q2W) for twelve 8-week treatment cycles.

Reporting group title	Part 3: PBO + Nivo 240
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Reporting group description:

Participants receive Placebo every 4 weeks (Q4W) and a flat dose of nivolumab monotherapy (240mg) every 2 weeks (Q2W) for 8-week cycles until progressive disease.

Reporting group title	Part 3: Liri 240 + Nivo 240
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Reporting group description:

Participants receive Lirilumab 240 mg every 4 weeks (Q4W) and a flat dose of nivolumab 240 mg every 2 weeks (Q2W) for 8-week cycles until progressive disease.

Reporting group title	Part 5: Liri 3 + Nivo 3 + Ipi 1
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Reporting group description:

Participants receive Lirilumab 3 mg/kg IV every 4 weeks (Q4W), Nivolumab 3 mg/kg IV every 2 weeks (Q2W), and Ipilimumab 1 mg/kg IV every 6 weeks (Q6W) for 12-week cycles until progressive disease

Serious adverse events	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	8 / 16 (50.00%)	9 / 15 (60.00%)
number of deaths (all causes)	2	7	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer metastatic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 in situ			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	2 / 16 (12.50%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aneurysm			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial rupture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Adverse drug reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Complication associated with device			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Secretion discharge			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Uterine polyp			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercapnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 disorder			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 hypertension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 distress			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 airway obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Completed suicide			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 Dislocation			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 placement issue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Head injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoradionecrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation skin injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 procedure complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Brain oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Coma			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 hernia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Autoimmune pancreatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland fistula			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-Abdominal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Hepatic cirrhosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Actinomycosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis orbital			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 externa			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (25.00%)	1 / 16 (6.25%)	0 / 15 (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
Pneumonia influenzal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Feeding disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Hyperkalaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (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
Malnutrition			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
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	Part 1/2: Liri 3 + Nivo 3	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240
Total subjects affected by serious adverse events			
subjects affected / exposed	205 / 287 (71.43%)	2 / 2 (100.00%)	3 / 3 (100.00%)
number of deaths (all causes)	219	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Breast cancer metastatic			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected neoplasm			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Malignant neoplasm progression			
subjects affected / exposed	109 / 287 (37.98%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	111 / 111	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Metastases to bone			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Tumour haemorrhage			

subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (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
Tumour pain			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Arterial rupture			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Embolism			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Hypertension			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Hypotension			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Shock haemorrhagic			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Thrombosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Asthenia			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (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
Complication associated with device			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (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
Fatigue			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	9 / 287 (3.14%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	10 / 10	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Localised oedema			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Malaise			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Pain			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	14 / 287 (4.88%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	16 / 17	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Secretion discharge			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Sudden death			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Swelling			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Ulcer			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Non-Cardiac chest pain			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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 pulmonary oedema			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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 respiratory failure			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Aspiration			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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	24 / 287 (8.36%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	24 / 25	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Haemoptysis			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (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
Hypercapnia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (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
Interstitial lung disease			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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 dyspnoea			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Lung disorder			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (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
Oropharyngeal pain			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Pharyngeal oedema			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (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
Pneumonia aspiration			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	8 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Respiratory distress			

subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper airway obstruction			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-Mediated pneumonitis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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			
Completed suicide			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Mental status changes			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Product issues			
Device occlusion			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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 Dislocation			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Investigations			

General physical condition abnormal subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (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
Lipase increased subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Clavicle fracture subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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 placement issue subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Head injury subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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

Hip fracture			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Infusion related reaction			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 13	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoradionecrosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Overdose			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Post procedural haemorrhage			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation skin injury			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Subdural haematoma			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Tracheal obstruction			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Vascular procedure complication			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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			
Arrhythmia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Atrial fibrillation			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Atrial flutter			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (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
Nervous system disorders			
Brain oedema			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery aneurysm			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Cerebral haemorrhage			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Dizziness			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolitic stroke			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Headache			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Hemiparesis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Neuropathy peripheral			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Presyncope			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Syncope			
subjects affected / exposed	2 / 287 (0.70%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	13 / 13	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Lymphadenopathy			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Splenic haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Thrombocytopenia			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Abdominal pain upper			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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 pancreatitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	8 / 8	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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 haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Haematemesis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Intestinal obstruction			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Mouth haemorrhage			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Nausea			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland fistula			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Small intestinal haemorrhage			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (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
Subileus			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Tongue haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-Abdominal haemorrhage			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Rash maculo-papular			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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			
Acute kidney injury			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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 failure			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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			
Arthralgia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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

Arthritis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Flank pain			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Muscular weakness			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Pathological fracture			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Actinomycosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Bacteraemia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Bronchitis			

subjects affected / exposed	0 / 287 (0.00%)	1 / 2 (50.00%)	0 / 3 (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
Cellulitis			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Cellulitis orbital			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Infective thrombosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Influenza			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
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 bacterial			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Lung abscess			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Osteomyelitis			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Pneumonia			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	13 / 13	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Sepsis			

subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	15 / 15	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Staphylococcal sepsis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Tracheitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (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
Dehydration			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Feeding disorder			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (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
Hypercalcaemia			
subjects affected / exposed	8 / 287 (2.79%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	10 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (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
Hypomagnesaemia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 5: Liri 3 + Nivo 3 + Ipi 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer metastatic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cancer pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected neoplasm				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma in situ				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm progression				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Malignant pleural effusion				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aneurysm			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arterial rupture			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shock			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Complication associated with device			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Face oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperthermia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised oedema				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Secretion discharge				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Swelling				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-Cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Dyspnoea exertional				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypercapnia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal dyspnoea				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngeal oedema				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper airway obstruction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-Mediated pneumonitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device occlusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device Dislocation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Lipase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device placement issue			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infusion related reaction				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoradionecrosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation skin injury				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stoma site haemorrhage				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheal obstruction				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular procedure complication			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tachycardia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carotid artery aneurysm			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central nervous system haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolic stroke			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone marrow failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymph node haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Splenic haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mouth haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Salivary gland fistula			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tongue haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-Abdominal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic haematoma			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Flank pain				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal wall abscess				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Actinomycosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis orbital				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective thrombosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection bacterial				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis externa				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psoas abscess				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tracheitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Feeding disorder				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1/2 Liri 0.1 + Nivo 3	Part 1/2: Liri 0.3 + Nivo 3	Part 1/2: Liri 1 + Nivo 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	16 / 16 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Acrochordon			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haemangioma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Seborrhoeic keratosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1

Melanocytic naevus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tumour haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	3 / 16 (18.75%)	0 / 15 (0.00%)
occurrences (all)	1	3	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	3
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Varicose vein			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	5 / 16 (31.25%)	1 / 15 (6.67%)
occurrences (all)	0	7	1
Device related thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Facial pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	6 / 16 (37.50%)	7 / 15 (46.67%)
occurrences (all)	4	6	9
Influenza like illness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	4
Injection site swelling			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Localised oedema			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Mass			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Nodule			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	3 / 15 (20.00%)
occurrences (all)	0	2	3
Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	5 / 16 (31.25%)	2 / 15 (13.33%)
occurrences (all)	1	7	2
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)	3 / 16 (18.75%)	1 / 15 (6.67%)
occurrences (all)	0	3	1
Xerosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Non-Cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Immune system disorders			

Hypersensitivity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Type iv hypersensitivity reaction subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Reproductive system and breast disorders			
Breast pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Uterine polyp subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Vulval disorder subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Vulva cyst subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Respiratory, thoracic and mediastinal disorders			
Atelectasis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2	9 / 16 (56.25%) 11	5 / 15 (33.33%) 6
Dysphonia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Dyspnoea			

subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Lung opacity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	3 / 16 (18.75%)	4 / 15 (26.67%)
occurrences (all)	0	10	6
Nasal mucosal disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pharyngeal disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pneumonia aspiration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	2 / 15 (13.33%)
occurrences (all)	0	1	3
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Immune-Mediated pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Depression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1

Depressed mood subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Hallucination subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Insomnia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	6 / 15 (40.00%) 9
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Amylase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 16 (12.50%) 2	1 / 15 (6.67%) 1
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 16 (18.75%) 3	0 / 15 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 16 (12.50%) 2	0 / 15 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	2 / 15 (13.33%) 2
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Blood magnesium decreased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Blood magnesium increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Blood phosphorus decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood testosterone decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Heart sounds abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Intraocular pressure increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Prothrombin time ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Troponin increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Cd4 lymphocytes decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram qt prolonged			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram t wave amplitude decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Incision site pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	7 / 15 (46.67%)
occurrences (all)	1	1	9
Muscle strain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Post procedural complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Wound dehiscence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Post-Traumatic pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Consciousness fluctuating			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dizziness			

subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	4 / 15 (26.67%)
occurrences (all)	0	2	6
Dysarthria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Facial paresis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hemiplegia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 4 (25.00%)	3 / 16 (18.75%)	4 / 15 (26.67%)
occurrences (all)	2	7	13
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	6
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Myoclonus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	5 / 15 (33.33%)
occurrences (all)	0	1	7
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinus headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Visual field defect			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Vith nerve paralysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	3 / 16 (18.75%)	0 / 15 (0.00%)
occurrences (all)	1	5	0
Eosinophilia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lymph node pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	2 / 15 (13.33%)
occurrences (all)	0	1	2

Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	1 / 15 (6.67%) 1
Ear and labyrinth disorders External ear pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Hypoacusis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	1 / 15 (6.67%) 1
Cataract nuclear subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Chorioretinal atrophy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Chorioretinal disorder subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Diplopia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eye movement disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Lagophthalmos			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Myopia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ocular discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Retinal deposits			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Strabismus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Swelling of eyelid			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Uveitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vision blurred			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vitreous detachment			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	2 / 16 (12.50%)	5 / 15 (33.33%)
occurrences (all)	1	2	6
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	3
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Anal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	5 / 16 (31.25%)	4 / 15 (26.67%)
occurrences (all)	0	6	4

Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	7 / 15 (46.67%)
occurrences (all)	0	4	20
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	3 / 16 (18.75%)	7 / 15 (46.67%)
occurrences (all)	3	4	16
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Oesophagitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oral disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	2 / 16 (12.50%)	5 / 15 (33.33%)
occurrences (all)	2	5	6
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Melanocytic hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Parapsoriasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	2 / 4 (50.00%)	4 / 16 (25.00%)	8 / 15 (53.33%)
occurrences (all)	2	7	11
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 4 (25.00%)	7 / 16 (43.75%)	4 / 15 (26.67%)
occurrences (all)	2	12	7
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	2 / 15 (13.33%)
occurrences (all)	0	2	3
Rash papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Scab			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Rash pruritic			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	4 / 15 (26.67%) 4
Skin hyperpigmentation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Skin lesion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Vitiligo subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	2 / 15 (13.33%) 2
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Nocturia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	2 / 15 (13.33%) 2
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Urinary retention subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Hypothyroidism			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	5 / 16 (31.25%)	8 / 15 (53.33%)
occurrences (all)	1	8	13
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	3 / 15 (20.00%)
occurrences (all)	1	1	5
Foot deformity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	6 / 15 (40.00%)
occurrences (all)	0	2	7
Musculoskeletal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 16 (6.25%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Musculoskeletal pain			

subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	0	6
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Pain in jaw			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	4 / 15 (26.67%)
occurrences (all)	0	2	7
Plantar fasciitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Fungal disease carrier			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Genital infection fungal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Pneumonia influenzal subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	3 / 16 (18.75%) 4	2 / 15 (13.33%) 2
Staphylococcal bacteraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	3 / 16 (18.75%) 3	2 / 15 (13.33%) 2
Viral infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 3	2 / 16 (12.50%) 2	4 / 15 (26.67%) 4
Dehydration subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 16 (6.25%) 1	2 / 15 (13.33%) 2
Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0
Gout subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0
Hyperglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	6
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	3
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	1 / 15 (6.67%)
occurrences (all)	0	1	3
Iron deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Non-serious adverse events	Part 1/2: Liri 3 + Nivo 3	Part 3: PBO + Nivo 240	Part 3: Liri 240 + Nivo 240
Total subjects affected by non-serious adverse events			
subjects affected / exposed	271 / 287 (94.43%)	2 / 2 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acrochordon			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemangioma			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic keratosis			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tumour haemorrhage			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	6	0	1
Tumour pain			
subjects affected / exposed	16 / 287 (5.57%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	16	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Embolism			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Hot flush			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypotension			
subjects affected / exposed	19 / 287 (6.62%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	20	0	2
Hypertension			
subjects affected / exposed	14 / 287 (4.88%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	14	0	0

Lymphoedema			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Thrombosis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	43 / 287 (14.98%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	57	0	0
Catheter site haemorrhage			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Chills			
subjects affected / exposed	31 / 287 (10.80%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	33	0	0
Device related thrombosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Early satiety			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	15 / 287 (5.23%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	17	0	0
Facial pain			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	144 / 287 (50.17%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	184	1	2
Influenza like illness			

subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Injection site swelling			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Malaise			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Mass			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	17 / 287 (5.92%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	17	0	0
Nodule			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	29 / 287 (10.10%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	31	0	0
Pain			
subjects affected / exposed	8 / 287 (2.79%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Peripheral swelling			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	69 / 287 (24.04%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	103	0	0
Swelling face			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Xerosis			

subjects affected / exposed occurrences (all)	5 / 287 (1.74%) 5	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Non-Cardiac chest pain subjects affected / exposed occurrences (all)	9 / 287 (3.14%) 11	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	3 / 287 (1.05%) 3	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Type iv hypersensitivity reaction subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Uterine polyp subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Vulval disorder subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Vulva cyst subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all)	2 / 287 (0.70%) 2	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Cough			

subjects affected / exposed	62 / 287 (21.60%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	73	0	0
Dysphonia			
subjects affected / exposed	18 / 287 (6.27%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	19	0	0
Dyspnoea			
subjects affected / exposed	47 / 287 (16.38%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	52	0	0
Dyspnoea exertional			
subjects affected / exposed	8 / 287 (2.79%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Haemoptysis			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	13	0	1
Lung opacity			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			
subjects affected / exposed	12 / 287 (4.18%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	12	0	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	7 / 287 (2.44%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	8	1	1
Paranasal sinus hypersecretion			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pharyngeal disorder			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	9 / 287 (3.14%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Pleuritic pain			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumonia aspiration			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Pneumonitis			
subjects affected / exposed	11 / 287 (3.83%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	12	0	1
Productive cough			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	15	0	0
Pulmonary embolism			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Respiratory tract congestion			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Sinus congestion			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Wheezing			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	9	0	0
Immune-Mediated pneumonitis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	8 / 287 (2.79%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0

Anxiety			
subjects affected / exposed	19 / 287 (6.62%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	20	0	0
Depression			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	13	0	0
Depressed mood			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	15 / 287 (5.23%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	15	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	19	0	0
Amylase increased			
subjects affected / exposed	19 / 287 (6.62%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	20	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 287 (7.32%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	28	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Blood bilirubin increased			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Blood creatinine increased			
subjects affected / exposed	17 / 287 (5.92%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	25	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood magnesium increased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood testosterone decreased			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Heart sounds abnormal			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intraocular pressure increased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Lipase increased			
subjects affected / exposed	21 / 287 (7.32%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	27	1	0
Neutrophil count decreased			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Transaminases increased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Prothrombin time ratio increased			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	39 / 287 (13.59%)	0 / 2 (0.00%)	3 / 3 (100.00%)
occurrences (all)	44	0	3
Troponin increased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Cd4 lymphocytes decreased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram t wave amplitude decreased			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Incision site pain			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	22 / 287 (7.67%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	24	0	0
Muscle strain			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			

subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Road traffic accident subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Skin abrasion subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Sunburn subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Wound dehiscence subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Post-Traumatic pain subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	7 / 287 (2.44%) 7	1 / 2 (50.00%) 1	0 / 3 (0.00%) 0
Cardiac failure subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	5 / 287 (1.74%) 5	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	9 / 287 (3.14%) 9	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders Burning sensation subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Cerebrovascular accident			

subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Consciousness fluctuating			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	22 / 287 (7.67%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	28	0	0
Dysarthria			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Facial paresis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hemiplegia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	44 / 287 (15.33%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	52	0	0
Hypoaesthesia			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Lethargy			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Memory impairment			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Myoclonus			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			

subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Paraesthesia			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Sinus headache			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Taste disorder			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Visual field defect			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Vith nerve paralysis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	70 / 287 (24.39%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	87	0	2
Eosinophilia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Lymph node pain subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 2	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	8 / 287 (2.79%) 18	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	2 / 287 (0.70%) 2	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders External ear pain subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Hypoacusis subjects affected / exposed occurrences (all)	3 / 287 (1.05%) 3	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	4 / 287 (1.39%) 4	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Cataract nuclear subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0	0 / 2 (0.00%) 0	0 / 3 (0.00%) 0
Chorioretinal atrophy			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chorioretinal disorder			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Dry eye			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Eye movement disorder			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lagophthalmos			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myopia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Retinal deposits			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling of eyelid			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Visual acuity reduced			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Visual impairment			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Vitreous detachment			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Abdominal distension			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Abdominal pain			
subjects affected / exposed	24 / 287 (8.36%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	29	0	0
Abdominal pain lower			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	9 / 287 (3.14%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	9	0	0
Anal haemorrhage			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Colitis			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Constipation			
subjects affected / exposed	60 / 287 (20.91%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	69	0	0
Dental caries			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			
subjects affected / exposed	66 / 287 (23.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	93	0	0
Dry mouth			
subjects affected / exposed	19 / 287 (6.62%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	22	0	0
Dyspepsia			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Dysphagia			
subjects affected / exposed	29 / 287 (10.10%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	32	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0

Nausea			
subjects affected / exposed	62 / 287 (21.60%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	75	0	1
Odynophagia			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	6	0	1
Oesophagitis			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Oral disorder			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Stomatitis			
subjects affected / exposed	10 / 287 (3.48%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	10	0	0
Toothache			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Vomiting			
subjects affected / exposed	43 / 287 (14.98%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	55	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Dermatitis acneiform			
subjects affected / exposed	4 / 287 (1.39%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Dry skin			

subjects affected / exposed	12 / 287 (4.18%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	13	0	0
Ecchymosis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	17 / 287 (5.92%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	17	0	0
Melanocytic hyperplasia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Parapsoriasis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	48 / 287 (16.72%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	65	0	0
Purpura			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	42 / 287 (14.63%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	61	0	0
Rash erythematous			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	13 / 287 (4.53%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	14	1	0
Rash papular			

subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Scab			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Skin hyperpigmentation			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Skin lesion			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Vitiligo			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Urinary incontinence			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
Hypothyroidism			
subjects affected / exposed	25 / 287 (8.71%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	31	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	35 / 287 (12.20%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	39	0	0
Arthritis			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Back pain			
subjects affected / exposed	34 / 287 (11.85%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	36	0	0
Foot deformity			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	15 / 287 (5.23%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	16	0	0
Muscular weakness			
subjects affected / exposed	6 / 287 (2.09%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Musculoskeletal discomfort			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal chest pain			

subjects affected / exposed	9 / 287 (3.14%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	9	0	0
Musculoskeletal pain			
subjects affected / exposed	15 / 287 (5.23%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	17	0	0
Musculoskeletal stiffness			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	11 / 287 (3.83%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	11	0	0
Osteoarthritis			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neck pain			
subjects affected / exposed	26 / 287 (9.06%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	27	0	0
Pain in jaw			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Pain in extremity			
subjects affected / exposed	8 / 287 (2.79%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	11 / 287 (3.83%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	13	0	0
Conjunctivitis			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0

Ear infection			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Fungal disease carrier			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Genital infection fungal			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	5 / 287 (1.74%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0

Pneumonia			
subjects affected / exposed	16 / 287 (5.57%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	19	1	0
Pneumonia influenzal			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	2 / 287 (0.70%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	18 / 287 (6.27%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	21	0	0
Viral infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	50 / 287 (17.42%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	55	0	1
Dehydration			
subjects affected / exposed	17 / 287 (5.92%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	21	0	1
Diabetes mellitus			
subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	21 / 287 (7.32%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	30	0	1
Gout			

subjects affected / exposed	0 / 287 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	13 / 287 (4.53%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	16	0	0
Hyperkalaemia			
subjects affected / exposed	9 / 287 (3.14%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	10	0	1
Hypoglycaemia			
subjects affected / exposed	3 / 287 (1.05%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	27 / 287 (9.41%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	44	0	0
Hypokalaemia			
subjects affected / exposed	22 / 287 (7.67%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	27	0	1
Hypophosphataemia			
subjects affected / exposed	14 / 287 (4.88%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	19	0	1
Hyponatraemia			
subjects affected / exposed	28 / 287 (9.76%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	34	0	0
Iron deficiency			
subjects affected / exposed	7 / 287 (2.44%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
Vitamin d deficiency			
subjects affected / exposed	1 / 287 (0.35%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part 5: Liri 3 + Nivo 3 + Ipi 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Acrochordon			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haemangioma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Seborrhoeic keratosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Melanocytic naevus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tumour haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Embolism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypotension			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Varicose vein			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Catheter site haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Device related thrombosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Early satiety			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Face oedema			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Facial pain			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Localised oedema			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	10		
Malaise			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mass			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nodule			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pyrexia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Swelling face</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Xerosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Non-Cardiac chest pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 10 (10.00%)</p> <p>1</p> <p>1 / 10 (10.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>		
<p>Immune system disorders</p> <p>Hypersensitivity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Type iv hypersensitivity reaction</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>		
<p>Reproductive system and breast disorders</p> <p>Breast pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Menstruation irregular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Uterine polyp</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vaginal haemorrhage</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vulval disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vulva cyst</p>	<p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>		

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	5		
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lung opacity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nasal mucosal disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Paranasal sinus hypersecretion			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pharyngeal disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pleuritic pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonia aspiration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Wheezing			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Immune-Mediated pneumonitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2		
Anxiety subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Depression subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Depressed mood subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hallucination subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Amylase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood magnesium decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood magnesium increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood testosterone decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Heart sounds abnormal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Intraocular pressure increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Lipase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Prothrombin time ratio increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Troponin increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cd4 lymphocytes decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Electrocardiogram t wave amplitude decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Incision site pain			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Post procedural complication			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Skin abrasion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Wound dehiscence			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Post-Traumatic pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac failure			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Tachycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cerebrovascular accident			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Consciousness fluctuating			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dysarthria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Facial paresis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hemiplegia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Memory impairment			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Myoclonus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinus headache			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Taste disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual field defect			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vith nerve paralysis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Agranulocytosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lymph node pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
External ear pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoacusis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vertigo			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cataract nuclear			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chorioretinal atrophy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chorioretinal disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry eye			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye movement disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lagophthalmos			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Meibomian gland dysfunction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Myopia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Ocular discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Retinal deposits			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Strabismus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Swelling of eyelid			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Uveitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vitreous detachment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal pain			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Colitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Dental caries			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Epigastric discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastritis			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Melaena			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oesophagitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oral disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Proctalgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			

Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Melanocytic hyperplasia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Parapsoriasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Papule			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	5		
Purpura			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Rash			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Rash erythematous			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Rash papular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Scab			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin hyperpigmentation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vitiligo			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nocturia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nephrolithiasis			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Arthritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Foot deformity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Joint stiffness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Joint swelling			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Plantar fasciitis			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fungal disease carrier			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Genital infection fungal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hordeolum			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Ophthalmic herpes zoster subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2		
Pneumonia influenzal subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Sinusitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Staphylococcal bacteraemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Viral infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite			

subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Diabetes mellitus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypercalcaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gout			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Iron deficiency			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vitamin d deficiency			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2012	Revised dose escalation design 3 + 3 + 3. Revised permanent discontinuation criteria. Revised eligibility to require subjects to have normal thyroid function and at least 1 prior therapy in the advanced/metastatic setting.
06 February 2014	In the dose escalation cohorts, increased the number of subjects that may be enrolled at each Dose Level from 12 to 15 in order to obtain additional data. Updated safety information for nivolumab and lirilumab. Additional tumor types of SCCHN and hepatocellular carcinoma added to dose cohort expansions. The colorectal cancer cohort was modified to enroll only subjects with non-microsatellite-instability-high tumors. Gehan 2-stage approach for efficacy assessment of these tumor types added. Cohort expansions of ovarian and renal cell carcinoma deleted. Inclusion criteria for all cohort expansions updated. Increased number of subjects in non-small cell lung cancer and melanoma cohorts. Updates to vital sign assessments, clarifications of efficacy criteria, and ADA endpoints were added.
24 July 2014	Updated inclusion and exclusion criteria, clarification of diagnostic imaging scan criteria and collection timelines, and addition of PK collection points.
02 November 2015	Add additional subjects to the SCCHN cohort in order to further explore the safety and efficacy of the compound.
12 April 2016	Updated objectives
12 December 2016	Indicated that the Dose Escalation and Cohort Expansion (Part 1) and the SCCHN Cohort Expansion (Part 2) have both completed enrollment and are not applicable starting with Amendment 13 and all subsequent amendments and that their specific eligibility criteria are not applicable. Added 4 new study parts: The SCCHN Randomized Cohorts (Part 3), The Signal Detection Cohort Expansion (Part 4), The Signal Detection in SCCHN with Lirilumab, Nivolumab, and Ipilimumab Combination (Part 5), The Signal Detection in Previously Untreated MEL with Lirilumab, Nivolumab, and Ipilimumab Combination (Part 6). Added that enrollment for the SCCHN Cohort Expansion (Part 2) will stop when the SCCHN Randomized Cohorts (Part 3) open. Safety text, eligibility criteria, study objectives, study design, discontinuation criteria, and statistical analyses updated for all new cohorts.
28 February 2017	Updated the cohort size and subject allocation for the Signal Detection Cohort Expansion (Part 4) and the cohort size, randomization scheme, treatment regimen, and inclusion criteria for the Signal Detection in Squamous Cell Carcinoma of the Head and Neck (SCCHN) with Lirilumab, Nivolumab, and Ipilimumab Combination (Part 5).
08 May 2018	The primary purpose of this revised protocol is to close the future enrollment in Part 3 and Part 5 and removal of Part 4 and Part 6 from the protocol study design.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported