# 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 |

### 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 | Italy: 38 |
| Country: Number of subjects enrolled | Spain: 3 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 190 |
| 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 |

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:<br>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:<br>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-comliance | - | 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-comliance | 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 | - | - |

| **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-comliance | - |
| 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)<br>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<br>Units: Years | | | |
| arithmetic mean | 59.7 | 65.5 | 55.3 |
| standard deviation | ± 11.37 | ± 10.61 | ± 21.08 |
| Sex: Female, Male<br>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)<br>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<br>Units: Years | | | |
| arithmetic mean | 67.1 | | |
| standard deviation | ± 10.40 | - | |

| | | | |
|---|---|---|---|
| Sex: Female, Male<br>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)<br>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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

End point description:

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

| 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:

[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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 >=50% or >=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 >= 50% and >= 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 >=50% TUMOR REDUCTION | 1 | 2 | 0 | |
| WITH >=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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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] |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

End point description:

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

| End point type | Secondary |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 >=1% or >= 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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 (± 99999) | | | |

## 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] |
|---|---|

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 |
|---|---|

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 (± 21) | 1155363.50 (± 33) | 4462883.03 (± 35) | 11418017.10 (± 28) |
| Cycle 2 | 569516.79 (± 26) | 1726615.52 (± 44) | 6712959.58 (± 31) | 18504162.18 (± 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 (± 99999) | | | |
| Cycle 2 | 99999 (± 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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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, 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 | | | |
|---|---|---|---|---|

| 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 (Vz) - Parts 1, 2 and 5

| End point title | Apparent Volume of Distribution During Terminal Phase (Vz) - Parts 1, 2 and 5[45] |
|---|---|

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 Vz are not reportable

| End point type | Secondary |
|---|---|

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 | () | | | |

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

### 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

| 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 |
| Embolic 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 | | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|
| 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 | | |

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|---|---|---|---|---|
| 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 | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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 | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|---|
| 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) | | | |
| Acrochordon | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Haemangioma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Melanocytic naevus | | | |
| 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 |
| 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 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 16 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 0 | 3 |
| 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 | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Type iv hypersensitivity reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vulva cyst | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vulval disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 9 / 16 (56.25%) | 5 / 15 (33.33%) |
| occurrences (all) | 2 | 11 | 6 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 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 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 3 |
| 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 | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 16 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Depression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 6 / 15 (40.00%) |
| occurrences (all) | 0 | 0 | 9 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 16 (12.50%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 16 (18.75%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 16 (12.50%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 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 phosphorus decreased | | | |
| 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 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 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 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 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 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 decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 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 |
| Headache | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 16 (18.75%) | 4 / 15 (26.67%) |
| occurrences (all) | 2 | 7 | 13 |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| 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 |
| Migraine | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Myoclonus | | | |
| 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 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 16 (12.50%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Melanocytic hyperplasia | | | |
| 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 |
| Parapsoriasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| 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 papular | | | |
| 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 |
| 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 | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 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 chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 1 | 2 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| 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 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 16 (12.50%) | 4 / 15 (26.67%) |
| occurrences (all) | 0 | 2 | 7 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| 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 | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 16 (18.75%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 4 | 2 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 16 (18.75%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 3 | 2 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 16 (12.50%) | 4 / 15 (26.67%) |
| occurrences (all) | 3 | 2 | 4 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 16 (6.25%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 1 | 2 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 16 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 0 | 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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 16 (6.25%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 | 3 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 16 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 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) | | | |
| Acrochordon | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| 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 |
| Melanocytic naevus | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 3 / 287 (1.05%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 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 |
| Hypertension | | | |
| subjects affected / exposed | 14 / 287 (4.88%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 14 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 19 / 287 (6.62%) | 0 / 2 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 20 | 0 | 2 |

| | | | |
|---|---|---|---|
| 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 | 5 / 287 (1.74%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Non-Cardiac chest pain | | | |
| subjects affected / exposed | 9 / 287 (3.14%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 11 | 0 | 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 3 / 287 (1.05%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Type iv hypersensitivity reaction | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulva cyst | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulval disorder | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Atelectasis | | | |
| subjects affected / exposed | 2 / 287 (0.70%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 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 |
| Wheezing | | | |
| subjects affected / exposed | 7 / 287 (2.44%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 5 / 287 (1.74%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 7 | 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 | | | |
| Anxiety | | | |
| subjects affected / exposed | 19 / 287 (6.62%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 20 | 0 | 0 |

| | | | |
|---|---|---|---|
| Confusional state | | | |
| subjects affected / exposed | 8 / 287 (2.79%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 13 / 287 (4.53%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 13 | 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 phosphorus decreased | | | |
| 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 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 |
| Lipase increased | | | |
| subjects affected / exposed | 21 / 287 (7.32%) | 1 / 2 (50.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 27 | 1 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 5 / 287 (1.74%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 287 (1.05%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 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 |
| Transaminases increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 39 / 287 (13.59%) | 0 / 2 (0.00%) | 3 / 3 (100.00%) |
| occurrences (all) | 44 | 0 | 3 |
| 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 | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post-Traumatic pain | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 7 / 287 (2.44%) | 1 / 2 (50.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 7 | 1 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 5 / 287 (1.74%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 9 / 287 (3.14%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 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 |
| Headache | | | |
| subjects affected / exposed | 44 / 287 (15.33%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 52 | 0 | 0 |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 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 |
| Migraine | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myoclonus | | | |
| 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 |

| | | | |
|---|---|---|---|
| Leukopenia | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 8 / 287 (2.79%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 18 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 287 (0.70%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| External ear pain | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 3 / 287 (1.05%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 4 / 287 (1.39%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cataract nuclear | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 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 | | | |
| Alopecia | | | |
| subjects affected / exposed | 4 / 287 (1.39%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 4 / 287 (1.39%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Ecchymosis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 12 / 287 (4.18%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 13 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 17 / 287 (5.92%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 17 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 6 / 287 (2.09%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Melanocytic hyperplasia | | | |
| 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 |
| Parapsoriasis | | | |
| subjects affected / exposed | 0 / 287 (0.00%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 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 papular | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 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 |
| 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 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 287 (0.35%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nocturia | | | |
| 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 chest pain | | | |
| subjects affected / exposed | 9 / 287 (3.14%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Musculoskeletal discomfort | | | |

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|---|---|---|---|
| subjects affected / exposed | 3 / 287 (1.05%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 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 |
| Neck pain | | | |
| subjects affected / exposed | 26 / 287 (9.06%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 27 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 2 / 287 (0.70%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 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 |
| Pain in jaw | | | |
| subjects affected / exposed | 7 / 287 (2.44%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 7 | 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 |
| Gout | | | |
| 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 |
| 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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 22 / 287 (7.67%) | 0 / 2 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 27 | 0 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 27 / 287 (9.41%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 44 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 28 / 287 (9.76%) | 0 / 2 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 34 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 14 / 287 (4.88%) | 0 / 2 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 19 | 0 | 1 |
| 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) | | | |

| | | | |
|---|---|---|---|
| Acrochordon | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemangioma | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Seborrhoeic keratosis | | | |
| 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 | | |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| 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 | | | | |

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

| | | | |
|---|---|---|---|
| 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 | | | |

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|---|---|---|---|---|
| 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 | | | |
| Wheezing | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Sinus congestion | | | | |

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

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|---|---|---|---|---|
| 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 phosphorus decreased | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood pressure increased | | | | |
| 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 | | | |
| Lipase increased | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 1 | | | |

| | | | |
|---|---|---|---|
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Prothrombin time ratio increased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| 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 | | |
| Headache | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hemiplegia | | | |
| 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 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myoclonus | | | |
| 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<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | |
| Anaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Eosinophilia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>2 | | |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | |
| Ear and labyrinth disorders<br>External ear pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>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 | | | |

| | | | | |
|---|---|---|---|---|
| Alopecia | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Dermatitis | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Dermatitis acneiform | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Ecchymosis | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Dry skin | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Erythema | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Night sweats | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Melanocytic hyperplasia | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Papule | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Parapsoriasis | | | | |
| 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 papular | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | |
| occurrences (all) | 2 | | |
| 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 | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nocturia | | | |

| | | | |
|---|---|---|---|
| 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 chest pain | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Musculoskeletal discomfort | | | | |
| 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 | | | |
| Neck pain | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 2 | | | |
| Osteoarthritis | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Pain in extremity | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Pain in jaw | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 1 | | | |
| 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<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Ophthalmic herpes zoster<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>2 | | | |
| Pneumonia influenzal<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | | |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | | |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Staphylococcal bacteraemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 10 (20.00%)<br>2 | | | |
| Viral infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | | | |
| Metabolism and nutrition disorders<br>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 | | | |
| Gout | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Hypercalcaemia | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 1 | | | |
| 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 | | | |
| Hypokalaemia | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 1 | | | |
| Hypomagnesaemia | | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | | |
| occurrences (all) | 2 | | | |
| Hyponatraemia | | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | | |
| occurrences (all) | 2 | | | |
| Hypophosphataemia | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | | |
| occurrences (all) | 1 | | | |
| 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.<br>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