



Clinical trial results:

A Phase 1 Study Of Ramucirumab, a Human Monoclonal Antibody Against the Vascular Endothelial Growth Factor-2 (VEGFR-2) Receptor in Children With Refractory Solid Tumors, Including CNS Tumors

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-000364-30 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 16 July 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 30 June 2021 |
| First version publication date | 30 June 2021 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I4T-MC-JVDA |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02564198 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 15542 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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? | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 16 July 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety of the study drug known as ramucirumab in children with recurrent or refractory solid tumors including central nervous system (CNS) tumors.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 December 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 29 |
| Worldwide total number of subjects | 29 |
| EEA total number of subjects | 0 |

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) | 1 |
| Children (2-11 years) | 10 |
| Adolescents (12-17 years) | 14 |
| Adults (18-64 years) | 4 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Completers included participants who had progressive disease, death due to any cause or alive and on study at conclusion, but off treatment.

Period 1

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

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 8 mg/kg Ramucirumab (Part A) |

Arm description:

Participants received 8 milligram per kilogram [mg/kg] Ramucirumab administered as an intravenous infusion every 2 weeks (Q2W) with 3 doses per 42 day cycle.

| | |
|--|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ramucirumab |
| Investigational medicinal product code | |
| Other name | IMC-1121B, Cyramza, LY3009806 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 8 mg/kg Ramucirumab administered as an intravenous infusion.

| | |
|------------------|-------------------------------|
| Arm title | 12 mg/kg Ramucirumab (Part A) |
|------------------|-------------------------------|

Arm description:

Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle.

| | |
|--|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ramucirumab |
| Investigational medicinal product code | |
| Other name | IMC-1121B, Cyramza, LY3009806 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 12 mg/kg Ramucirumab administered as an intravenous infusion.

| | |
|------------------|-------------------------------|
| Arm title | 12 mg/kg Ramucirumab (Part B) |
|------------------|-------------------------------|

Arm description:

Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle.

| | |
|--|-------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ramucirumab |
| Investigational medicinal product code | |
| Other name | IMC-1121B, Cyramza, LY3009806 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 12 mg/kg Ramucirumab administered as an intravenous infusion.

| Number of subjects in period 1 | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) |
|--|------------------------------------|-------------------------------------|-------------------------------------|
| Started | 8 | 15 | 6 |
| Received at least 1 dose of study drug | 8 | 15 | 6 |
| Completed | 6 | 10 | 6 |
| Not completed | 2 | 5 | 0 |
| Consent withdrawn by subject | 2 | 4 | - |
| Adverse event, non-fatal | - | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|-------------------------------|
| Reporting group title | 8 mg/kg Ramucirumab (Part A) |
| Reporting group description: | |
| Participants received 8 milligram per kilogram [mg/kg] Ramucirumab administered as an intravenous infusion every 2 weeks (Q2W) with 3 doses per 42 day cycle. | |
| Reporting group title | 12 mg/kg Ramucirumab (Part A) |
| Reporting group description: | |
| Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle. | |
| Reporting group title | 12 mg/kg Ramucirumab (Part B) |
| Reporting group description: | |
| Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle. | |

| Reporting group values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) |
|---|------------------------------------|-------------------------------------|-------------------------------------|
| Number of subjects | 8 | 15 | 6 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 15.8 | 11.9 | 9.7 |
| standard deviation | ± 3.33 | ± 5.59 | ± 5.9 |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 6 | 2 |
| Male | 4 | 9 | 4 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 2 | 2 | 2 |
| Not Hispanic or Latino | 6 | 12 | 4 |
| Unknown or Not Reported | 0 | 1 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 2 | 1 |

| | | | |
|-------------------------|---|----|---|
| White | 7 | 12 | 4 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 1 | 1 | 1 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| United States | 8 | 15 | 6 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 29 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 12 | | |
| Male | 17 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 6 | | |
| Not Hispanic or Latino | 22 | | |
| Unknown or Not Reported | 1 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 3 | | |
| White | 23 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 3 | | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| United States | 29 | | |

End points

End points reporting groups

| | |
|---|-------------------------------|
| Reporting group title | 8 mg/kg Ramucirumab (Part A) |
| Reporting group description: Participants received 8 milligram per kilogram [mg/kg] Ramucirumab administered as an intravenous infusion every 2 weeks (Q2W) with 3 doses per 42 day cycle. | |
| Reporting group title | 12 mg/kg Ramucirumab (Part A) |
| Reporting group description: Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle. | |
| Reporting group title | 12 mg/kg Ramucirumab (Part B) |
| Reporting group description: Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle. | |
| Subject analysis set title | 8 mg/kg Ramucirumab |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received 8 mg/kg Ramucirumab administered as an intravenous infusion Q2W with 3 doses per 42 day cycle. | |
| Subject analysis set title | 12 mg/kg Ramucirumab |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received 12 mg/kg Ramucirumab as an intravenous injection Q2W with 3 doses per cycle. | |

Primary: Number of participants with Dose Limiting Toxicities (DLTs): Maximum Tolerated Dose of Ramucirumab

| | |
|--|--|
| End point title | Number of participants with Dose Limiting Toxicities (DLTs): Maximum Tolerated Dose of Ramucirumab ^{[1][2]} |
| End point description: A DLT is defined as an Adverse Event (AE) that is likely related to the study medication or combination, and fulfills any one of the following criteria, graded according to the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0: 1. Any death not clearly due to the underlying disease or extraneous causes 2. Neutropenic fever 2. Any Grade ≥ 3 non-hematologic toxicity 3. Grade ≥ 4 neutropenia or thrombocytopenia > 7 days 4. Grade ≥ 3 thrombocytopenia with bleeding 5. Grade ≥ 3 nausea/vomiting or diarrhea > 72 hours with adequate antiemetic and other supportive care 6. Grade ≥ 3 fatigue ≥ 1 week 7. Grade ≥ 3 electrolyte abnormality that lasts > 72 hours, unless the Participant has clinical symptoms, in which case all Grade 3+electrolyte abnormality regardless of duration should count as a DLT. Analysis Population Description (APD): All randomized participants who received at least one dose of study drug. | |
| End point type | Primary |
| End point timeframe: Baseline to Study Completion (Up to 42 Months) | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No inferential statistics were 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: No inferential statistics were planned for this endpoint. | |

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | | |
|-----------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 15 | | |
| Units: Participants | | | | |
| number (not applicable) | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Population Pharmacokinetics (PK): Minimum Concentration (Cmin) of Ramucirumab

| | |
|-----------------|--|
| End point title | Population Pharmacokinetics (PK): Minimum Concentration (Cmin) of Ramucirumab ^[3] |
|-----------------|--|

End point description:

Population Pharmacokinetics (PK): Minimum observed plasma concentration of Ramucirumab.

APD: All randomized participants who received at least one dose of study drug and had evaluable PK data.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Predose, Cycle 1 Day 1 (end of infusion (EOI), 1 hour after EOI) and Cycle 1 Day 43 (1 hour after EOI)

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: No inferential statistics were planned for this endpoint.

| End point values | 8 mg/kg Ramucirumab | 12 mg/kg Ramucirumab | | |
|---|------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 8 ^[4] | 19 ^[5] | | |
| Units: microgram per milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 Day 1 | 30.0 (± 32) | 48.3 (± 41) | | |
| Cycle 1 Day 43 | 53.6 (± 31) | 80.2 (± 44) | | |

Notes:

[4] - Cycle 1 Day 1: 8 participants

Cycle 1 Day 43: 4 participants

[5] - Cycle 1 Day 1: 19 participants

Cycle 1 Day 43: 16 participants

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Anti-Ramucirumab Antibodies

| | |
|-----------------|--|
| End point title | Number of Participants with Anti-Ramucirumab Antibodies ^[6] |
|-----------------|--|

End point description:

Number of participants with positive treatment emergent anti-ramucirumab antibodies was summarized by treatment group. A treatment-emergent anti-drug antibodies (TEADA) sample was defined as: a post

treatment sample with at least a 4-fold increase in titer from pre treatment sample; or 1:20 post treatment titer for participants that had no detectable ADA titer at baseline.

APD: All randomized participants who received at least one dose of study drug.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Predose Cycle 1 Day 1 through Follow-Up (Up to 42 Months) | |

Notes:

[6] - 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: No inferential statistics were planned for this endpoint.

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) | |
|-----------------------------|------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 15 | 6 | |
| Units: participants | | | | |
| number (not applicable) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR): Percentage of Participants Who Achieve Complete Response (CR) or Partial Response (PR)

| | |
|-----------------|---|
| End point title | Overall Response Rate (ORR): Percentage of Participants Who Achieve Complete Response (CR) or Partial Response (PR) |
|-----------------|---|

End point description:

ORR is the best response of complete response (CR) or partial response (PR) as classified by the independent central review according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1). CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of non-target lesions or appearance of new lesions. Overall response rate is calculated as a total number of participants with CR or PR divided by the total number of participants per cohort with at least 1 measurable lesion, multiplied by 100. Progressive Disease (PD) was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions.

APD: All randomized participants.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Date of Objective Disease Progression (Up to 42 Months) | |

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) | |
|-----------------------------------|------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 15 | 6 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0.0 to 41.0) | 0 (0.0 to 23.2) | 0 (0.0 to 45.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD): Disease Control Rate (DCR)

| | |
|-----------------|---|
| End point title | Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD): Disease Control Rate (DCR) |
|-----------------|---|

End point description:

Disease Control Rate (DCR) was the percentage of participants with a best overall response of CR, PR, or Stable Disease (SD) as per Response using RECIST v1.1 criteria. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. SD was neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD for target lesions, no progression of non-target lesions, and no appearance of new lesions. PD was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions.

APD: All randomized participants who received at least one dose of study drug.

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

End point timeframe:

Baseline to Date of Objective Disease Progression (Up to 42 Months)

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) | |
|-----------------------------------|------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 15 | 6 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 62.5 (29.0 to 96.3) | 40.0 (17.7 to 71.1) | 33.3 (4.3 to 77.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

| | |
|-----------------|----------------------------|
| End point title | Duration of Response (DOR) |
|-----------------|----------------------------|

End point description:

DOR was the time from the date of first evidence of complete response or partial response to the date of objective progression or the date of death due to any cause, whichever is earlier. CR and PR were

defined using the RECIST v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. If a responder was not known to have died or have objective progression as of the data inclusion cutoff date, duration of response was censored at the last adequate tumor assessment date.

APD: Zero participants analyzed. Duration of response was not evaluable, as there were no participants with CR or PR.

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

End point timeframe:

Date of Complete Response (CR) or Partial Response (PR) to Date of Objective Disease Progression or Death Due to Any Cause (Up to 42 Months)

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) | |
|----------------------------------|------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[7] | 0 ^[8] | 0 ^[9] | |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | (to) | (to) | |

Notes:

[7] - Writer To Revise

[8] - Writer To Revise

[9] - Writer To Revise

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall survival is defined as the time from date of randomization to the date of death (due to any cause). For participants whose last known status is alive at the data cutoff date for the analysis, time will be censored as the last contact date prior to the data cutoff date.

APD: Zero participants analyzed. Overall survival was not evaluable, as there were no deaths observed in this study.

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

End point timeframe:

Baseline to Date of Death from Any Cause (Up to 42 Months)

| End point values | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) | |
|----------------------------------|------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | 0 ^[12] | |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | (to) | (to) | |

Notes:

[10] - Writer To Revise

[11] - Writer To Revise

[12] - Writer To Revise

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline, up to 4 years 8 months

Adverse event reporting additional description:

I4T-MC-JVDA

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------------|
| Reporting group title | 8 mg/kg Ramucirumab (Part A) |
|-----------------------|------------------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------------|
| Reporting group title | 12 mg/kg Ramucirumab (Part A) |
|-----------------------|-------------------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------------|
| Reporting group title | 12 mg/kg Ramucirumab (Part B) |
|-----------------------|-------------------------------|

Reporting group description: -

| Serious adverse events | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) |
|---|------------------------------------|-------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 7 / 15 (46.67%) | 2 / 6 (33.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| tumour pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| fracture | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |

| | | | |
|---|----------------------------------|----------------------------------|----------------------------------|
| hypertension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 8 (12.50%) 0 / 1 0 / 0 | 0 / 15 (0.00%) 0 / 0 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| hypotension alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 8 (12.50%) 0 / 1 0 / 0 | 0 / 15 (0.00%) 0 / 0 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| Nervous system disorders headache alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 8 (12.50%) 0 / 1 0 / 0 | 0 / 15 (0.00%) 0 / 0 0 / 0 | 1 / 6 (16.67%) 0 / 1 0 / 0 |
| paraesthesia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| peripheral motor neuropathy alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| seizure alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 0 / 15 (0.00%) 0 / 0 0 / 0 | 1 / 6 (16.67%) 0 / 1 0 / 0 |
| General disorders and administration site conditions pyrexia | | | |

| | | | |
|--|---------------|-----------------|---------------|
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 15 (20.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoxia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pulmonary haemorrhage | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| urinary tract obstruction | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---------------------------------|----------------------------------|----------------------------------|
| bone pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| Infections and infestations infection alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |
| kidney infection alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 0 / 15 (0.00%) 0 / 0 0 / 0 | 1 / 6 (16.67%) 0 / 1 0 / 0 |
| pneumonia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 8 (0.00%) 0 / 0 0 / 0 | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 6 (0.00%) 0 / 0 0 / 0 |

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

| Non-serious adverse events | 8 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part A) | 12 mg/kg Ramucirumab (Part B) |
|--|------------------------------------|-------------------------------------|-------------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 8 / 8 (100.00%) | 15 / 15 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) tumour haemorrhage alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) tumour pain alternative dictionary used: | 1 / 8 (12.50%) 1 | 0 / 15 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|---|----------------|-----------------|----------------|
| MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| flushing | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| hypertension | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 6 / 15 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 13 | 3 |
| hypotension | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 15 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 8 | 2 |
| General disorders and administration site conditions | | | |
| chills | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| face oedema | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| facial pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| fatigue | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 8 / 15 (53.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 9 | 1 |
| impaired healing | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| localised oedema | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| malaise | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 6 / 15 (40.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 6 | 1 |
| swelling | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| hypersensitivity | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| aphonia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| aspiration | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| atelectasis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| cough | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 7 / 15 (46.67%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 10 | 3 |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 2 |
| epistaxis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| nasal congestion | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 5 / 15 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 5 | 1 |
| oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 15 (26.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 4 | 1 |
| productive cough | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|---------------------|----------------------|---------------------|
| rhinitis allergic alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 6 (0.00%) 0 |
| rhinorrhoea alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 15 (13.33%) 3 | 2 / 6 (33.33%) 2 |
| upper respiratory tract congestion alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 6 (0.00%) 0 |
| wheezing alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 6 (0.00%) 0 |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 15 (0.00%) 0 | 2 / 6 (33.33%) 2 |
| confusional state alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| depression alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 6 (0.00%) 0 |
| insomnia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 6 (0.00%) 0 |
| personality change alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|------------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Investigations | | | |
| activated partial thromboplastin time prolonged | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 6 / 15 (40.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 7 | 3 |
| anion gap increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 12 / 15 (80.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 14 | 2 |
| bacterial test positive | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 4 / 15 (26.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| blood bicarbonate decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| blood bilirubin increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| blood cholesterol increased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| blood creatinine increased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 2 |
| c-reactive protein increased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ejection fraction decreased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| haemoglobin increased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 3 / 6 (50.00%) |
| occurrences (all) | 2 | 6 | 5 |
| international normalised ratio decreased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| international normalised ratio increased alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| lipase increased alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| lymphocyte count decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 2 / 15 (13.33%) | 4 / 6 (66.67%) |
| occurrences (all) | 7 | 2 | 5 |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 5 / 15 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 6 | 2 |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 3 / 15 (20.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 4 | 3 |
| prothrombin time shortened | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| weight decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| weight increased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 5 | 2 |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 6 / 15 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 7 | 2 |
| Injury, poisoning and procedural complications | | | |
| arthropod bite | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| contusion | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| gastrostomy tube site complication | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| infusion related reaction | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| post procedural discharge | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| skin laceration | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| vascular access complication | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| sinus bradycardia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| sinus tachycardia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 2 / 8 (25.00%) | 5 / 15 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 7 | 3 |
| Nervous system disorders | | | |
| ataxia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| disturbance in attention | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| dizziness | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| headache | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 7 / 15 (46.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 8 | 0 |
| hemiparesis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| hypersomnia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| hypoesthesia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| memory impairment | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>sinus headache</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>somnolence</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 8 (0.00%)</p> <p>0</p> <p>1 / 8 (12.50%)</p> <p>1</p> <p>0 / 8 (0.00%)</p> <p>0</p> | <p>0 / 15 (0.00%)</p> <p>0</p> <p>0 / 15 (0.00%)</p> <p>0</p> <p>1 / 15 (6.67%)</p> <p>1</p> | <p>1 / 6 (16.67%)</p> <p>1</p> <p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>0</p> |
| <p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>eosinophilia</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 8 (25.00%)</p> <p>4</p> <p>0 / 8 (0.00%)</p> <p>0</p> | <p>9 / 15 (60.00%)</p> <p>9</p> <p>1 / 15 (6.67%)</p> <p>1</p> | <p>2 / 6 (33.33%)</p> <p>3</p> <p>0 / 6 (0.00%)</p> <p>0</p> |
| <p>Ear and labyrinth disorders</p> <p>ear pain</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypoacusis</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 8 (0.00%)</p> <p>0</p> <p>0 / 8 (0.00%)</p> <p>0</p> | <p>0 / 15 (0.00%)</p> <p>0</p> <p>1 / 15 (6.67%)</p> <p>1</p> | <p>1 / 6 (16.67%)</p> <p>1</p> <p>0 / 6 (0.00%)</p> <p>0</p> |
| <p>Eye disorders</p> <p>eye pain</p> <p>alternative dictionary used: MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>photophobia</p> <p>alternative dictionary used: MedDRA 23.0</p> | <p>0 / 8 (0.00%)</p> <p>0</p> | <p>2 / 15 (13.33%)</p> <p>2</p> | <p>0 / 6 (0.00%)</p> <p>0</p> |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| vision blurred | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 5 / 15 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 6 | 2 |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| constipation | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 2 | 3 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 1 | 2 |
| dysphagia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| mouth ulceration | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| nausea | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 7 / 15 (46.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 5 | 7 | 1 |
| oral disorder | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| periodontal disease | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| stomatitis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| tongue geographic | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| vomiting | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 7 / 15 (46.67%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 7 | 3 |
| Skin and subcutaneous tissue disorders | | | |
| alopecia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| dermatitis acneiform | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| dry skin | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| eczema asteatotic | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| erythema multiforme | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| onychomadesis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| pain of skin | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| petechiae | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| pruritus | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 2 | 1 |
| rash maculo-papular | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 15 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |

| | | | |
|--|---|--|---|
| skin ulcer alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 2 | 0 / 15 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Renal and urinary disorders chromaturia alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) haematuria alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) pollakiuria alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) proteinuria alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) urinary hesitation alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) urinary tract pain alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 2 / 8 (25.00%) 2 0 / 8 (0.00%) 0 2 / 8 (25.00%) 4 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 | 0 / 15 (0.00%) 0 4 / 15 (26.67%) 4 1 / 15 (6.67%) 1 6 / 15 (40.00%) 8 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1 | 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 |
| Endocrine disorders hyperthyroidism alternative dictionary used: MedDRA 23.0 subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 15 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| back pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| flank pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| myalgia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| neck pain | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| osteoporosis | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| pain in extremity | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|--|---------------------|----------------------|--------------------|
| subjects affected / exposed occurrences (all) | 3 / 8 (37.50%) 3 | 2 / 15 (13.33%) 5 | 0 / 6 (0.00%) 0 |
| Infections and infestations | | | |
| coxsackie viral infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| mucosal infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| skin infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| soft tissue infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 15 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 7 / 15 (46.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 9 | 2 |
| dehydration | | | |
| alternative dictionary used: MedDRA 23.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| hypercalcaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 5 / 15 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 8 | 2 |
| hyperkalaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 4 | 1 |
| hypermagnesaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 15 (26.67%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 4 | 4 |
| hypernatraemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| hyperphosphataemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 15 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 4 / 15 (26.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 6 | 1 |
| hypocalcaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 7 / 15 (46.67%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 7 | 3 |

| | | | |
|---|----------------|-----------------|----------------|
| hypochloraemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| hypoglycaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 15 (26.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 2 | 1 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 7 / 15 (46.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 12 | 1 |
| hypophosphataemia | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 5 / 15 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 5 | 3 |
| vitamin d deficiency | | | |
| alternative dictionary used: MedDRA 23.0 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported