



## Clinical trial results:

### A Randomized, Open-Label Phase 1/2 Study Evaluating Ramucirumab in Pediatric Patients and Young Adults With Relapsed, Recurrent, or Refractory Desmoplastic Small Round Cell Tumor

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2018-004242-42    |
| Trial protocol           | FR DE ES NL BE IT |
| Global end of trial date | 23 January 2026   |

#### Results information

|                                |                                                             |
|--------------------------------|-------------------------------------------------------------|
| Result version number          | v3 (current)                                                |
| This version publication date  | 31 July 2026                                                |
| First version publication date | 28 June 2025                                                |
| Version creation reason        | • Correction of full data set<br>For Final results postings |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | J1S-MC-JV01 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                     |
|------------------------------------|---------------------|
| ISRCTN number                      | -                   |
| ClinicalTrials.gov id (NCT number) | NCT04145349         |
| WHO universal trial number (UTN)   | -                   |
| Other trial identifiers            | Trial Number: 17305 |

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, 1 877-CTLilly,  |
| Scientific contact           | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

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                       | 23 January 2026 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 23 January 2026 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

This study is being conducted to test the safety and efficacy of ramucirumab in combination with other chemotherapy in the treatment of relapsed, recurrent, or refractory desmoplastic small round cell tumor (DSRCT) in children and young adults. This trial is part of the CAMPFIRE master protocol (NCT05999994) which is a platform to accelerate the development of new treatments for pediatric and young adult participants with cancer. Your participation in this trial could last 12 months or longer, depending on how you and your tumor respond.

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                          | 22 January 2020 |
| 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 | Spain: 3          |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | Germany: 3        |
| Country: Number of subjects enrolled | Italy: 4          |
| Country: Number of subjects enrolled | United States: 9  |
| Country: Number of subjects enrolled | Japan: 4          |
| Country: Number of subjects enrolled | Australia: 1      |
| Worldwide total number of subjects   | 30                |
| EEA total number of subjects         | 10                |

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)                    | 1  |
| Adolescents (12-17 years)                | 10 |
| Adults (18-64 years)                     | 19 |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Completers included participants who died due to any cause or were alive and on study at conclusion but off treatment.

### Pre-assignment

Screening details:

No Text Available

### Period 1

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

### Arms

|                              |                                              |
|------------------------------|----------------------------------------------|
| Are arms mutually exclusive? | Yes                                          |
| <b>Arm title</b>             | Ramucirumab + Cyclophosphamide + Vinorelbine |

Arm description:

Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

Ramucirumab administered intravenously at a dose of 12 milligrams per kilogram (mg/kg) as a one-hour infusion on days 1 and 15.

Cyclophosphamide administered orally at 25 milligrams per meter square (mg/m<sup>2</sup>) daily from days 1 to 28.

Vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Ramucirumab           |
| Investigational medicinal product code |                       |
| Other name                             | LY3009806             |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Participants received ramucirumab administered intravenously at a dose of 12 milligrams per kilogram (mg/kg) as a one-hour infusion on days 1 and 15 of a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Coated tablet    |
| Routes of administration               | Oral use         |

Dosage and administration details:

Participants received cyclophosphamide administered orally at 25 milligrams per meter square (mg/m<sup>2</sup>) daily from days 1 to 28 of a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Vinorelbine           |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Participants received vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15 of a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | Cyclophosphamide + Vinorelbine |
|------------------|--------------------------------|

**Arm description:**

Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

Cyclophosphamide administered orally at 25 mg/m<sup>2</sup> daily from days 1 to 28.

Vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Cyclophosphamide  |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Coated tablet     |
| Routes of administration               | Oral use          |

**Dosage and administration details:**

Participants received cyclophosphamide administered orally at 25 milligrams per meter square (mg/m<sup>2</sup>) daily from days 1 to 28 of a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Vinorelbine           |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Participants received vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15 of a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

| <b>Number of subjects in period 1</b>       | Ramucirumab +<br>Cyclophosphamide<br>+ Vinorelbine | Cyclophosphamide +<br>Vinorelbine |
|---------------------------------------------|----------------------------------------------------|-----------------------------------|
| Started                                     | 20                                                 | 10                                |
| Received at Least One Dose of Study<br>Drug | 20                                                 | 10                                |
| Completed                                   | 12                                                 | 7                                 |
| Not completed                               | 8                                                  | 3                                 |
| Consent withdrawn by subject                | 8                                                  | 2                                 |
| Lost to follow-up                           | -                                                  | 1                                 |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                    |                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Reporting group title                                                                                                                              | Ramucirumab + Cyclophosphamide + Vinorelbine |
| Reporting group description:                                                                                                                       |                                              |
| Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met. |                                              |
| Ramucirumab administered intravenously at a dose of 12 milligrams per kilogram (mg/kg) as a one-hour infusion on days 1 and 15.                    |                                              |
| Cyclophosphamide administered orally at 25 milligrams per meter square (mg/m <sup>2</sup> ) daily from days 1 to 28.                               |                                              |
| Vinorelbine administered intravenously at 25 mg/m <sup>2</sup> on days 1, 8, and 15.                                                               |                                              |
| Reporting group title                                                                                                                              | Cyclophosphamide + Vinorelbine               |
| Reporting group description:                                                                                                                       |                                              |
| Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met. |                                              |
| Cyclophosphamide administered orally at 25 mg/m <sup>2</sup> daily from days 1 to 28.                                                              |                                              |
| Vinorelbine administered intravenously at 25 mg/m <sup>2</sup> on days 1, 8, and 15.                                                               |                                              |

| Reporting group values | Ramucirumab + Cyclophosphamide + Vinorelbine | Cyclophosphamide + Vinorelbine | Total |
|------------------------|----------------------------------------------|--------------------------------|-------|
| Number of subjects     | 20                                           | 10                             | 30    |
| Age categorical        |                                              |                                |       |
| Units: Subjects        |                                              |                                |       |

|                                           |        |        |    |
|-------------------------------------------|--------|--------|----|
| Age continuous                            |        |        |    |
| Units: years                              |        |        |    |
| arithmetic mean                           | 19.6   | 21.4   |    |
| standard deviation                        | ± 5.67 | ± 5.06 | -  |
| Gender categorical                        |        |        |    |
| Units: Subjects                           |        |        |    |
| Female                                    | 5      | 0      | 5  |
| Male                                      | 15     | 10     | 25 |
| Ethnicity (NIH/OMB)                       |        |        |    |
| Units: Subjects                           |        |        |    |
| Hispanic or Latino                        | 3      | 1      | 4  |
| Not Hispanic or Latino                    | 16     | 8      | 24 |
| Unknown or Not Reported                   | 1      | 1      | 2  |
| Race (NIH/OMB)                            |        |        |    |
| Units: Subjects                           |        |        |    |
| American Indian or Alaska Native          | 0      | 0      | 0  |
| Asian                                     | 2      | 4      | 6  |
| Native Hawaiian or Other Pacific Islander | 0      | 0      | 0  |
| Black or African American                 | 4      | 1      | 5  |
| White                                     | 13     | 4      | 17 |
| More than one race                        | 0      | 0      | 0  |
| Unknown or Not Reported                   | 1      | 1      | 2  |
| Region of Enrollment                      |        |        |    |
| Units: Subjects                           |        |        |    |
| United States                             | 5      | 4      | 9  |

|                |   |   |   |
|----------------|---|---|---|
| Japan          | 1 | 3 | 4 |
| Italy          | 3 | 1 | 4 |
| United Kingdom | 5 | 1 | 6 |
| Australia      | 1 | 0 | 1 |
| Germany        | 3 | 0 | 3 |
| Spain          | 2 | 1 | 3 |

## End points

### End points reporting groups

|                                                                                                                                                    |                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Reporting group title                                                                                                                              | Ramucirumab + Cyclophosphamide + Vinorelbine |
| Reporting group description:                                                                                                                       |                                              |
| Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met. |                                              |
| Ramucirumab administered intravenously at a dose of 12 milligrams per kilogram (mg/kg) as a one-hour infusion on days 1 and 15.                    |                                              |
| Cyclophosphamide administered orally at 25 milligrams per meter square (mg/m <sup>2</sup> ) daily from days 1 to 28.                               |                                              |
| Vinorelbine administered intravenously at 25 mg/m <sup>2</sup> on days 1, 8, and 15.                                                               |                                              |
| Reporting group title                                                                                                                              | Cyclophosphamide + Vinorelbine               |
| Reporting group description:                                                                                                                       |                                              |
| Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met. |                                              |
| Cyclophosphamide administered orally at 25 mg/m <sup>2</sup> daily from days 1 to 28.                                                              |                                              |
| Vinorelbine administered intravenously at 25 mg/m <sup>2</sup> on days 1, 8, and 15.                                                               |                                              |

### Primary: Progression Free Survival (PFS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Progression Free Survival (PFS) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                 |
| PFS was defined as the time from randomization to the date of investigator-determined objective progression as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, or death from any cause in the absence of disease progression. Progressive disease (PD) was defined as 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. Participants known to be alive and without disease progression were censored at the date of their last adequate tumor assessment per RECIST 1.1 criteria, or date of randomization (whichever is later). Data are presented as the posterior median with 98% credible interval estimated using Bayesian analysis. Analysis Population Description (APD): All randomized participants who received at least 1 dose of study drug (including the censored participants). |                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Primary                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                 |
| Randomization to Objective Progression or Death Due to Any Cause (Up To 23 Months)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                 |

| End point values                 | Ramucirumab + Cyclophosphamide + Vinorelbine | Cyclophosphamide + Vinorelbine |  |  |
|----------------------------------|----------------------------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group                              | Reporting group                |  |  |
| Number of subjects analysed      | 20 <sup>[1]</sup>                            | 10 <sup>[2]</sup>              |  |  |
| Units: Months                    |                                              |                                |  |  |
| median (confidence interval 98%) | 5.69 (3.20 to 10.01)                         | 3.73 (1.76 to 8.29)            |  |  |

Notes:

[1] - Number of participants censored in Ramucirumab + Cyclophosphamide + Vinorelbine = 4

[2] - Number of participants censored in Cyclophosphamide + Vinorelbine = 2

### Statistical analyses

|                                                                                                                                                                  |                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                | Statistical Analysis 1                                                           |
| Statistical analysis description:<br>The Bayesian analyses below include posterior mean of Hazard ratio, and credible intervals instead of confidence intervals. |                                                                                  |
| Comparison groups                                                                                                                                                | Ramucirumab + Cyclophosphamide + Vinorelbine v<br>Cyclophosphamide + Vinorelbine |
| Number of subjects included in analysis                                                                                                                          | 30                                                                               |
| Analysis specification                                                                                                                                           | Pre-specified                                                                    |
| Analysis type                                                                                                                                                    | superiority <sup>[3]</sup>                                                       |
| Method                                                                                                                                                           | Bayesian hierarchical model                                                      |
| Parameter estimate                                                                                                                                               | Posterior Mean Hazard Ratio                                                      |
| Point estimate                                                                                                                                                   | 0.69                                                                             |
| Confidence interval                                                                                                                                              |                                                                                  |
| level                                                                                                                                                            | Other: 98 %                                                                      |
| sides                                                                                                                                                            | 2-sided                                                                          |
| lower limit                                                                                                                                                      | 0.25                                                                             |
| upper limit                                                                                                                                                      | 1.69                                                                             |

Notes:

[3] - The posterior probability treatment difference is 0.864

### **Secondary: Overall Response Rate (ORR): Percentage of Participants Who Achieved a Complete Response (CR) or Partial Response (PR)**

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

End point description:

The ORR was defined as the percentage of participants achieving either a CR or PR. Tumor response was assessed based on histology: Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) was used for solid tumors, and Response Assessment in Neuro-Oncology criteria were used for glioblastoma. CR was defined as the disappearance of all target lesions, with any pathological lymph nodes (whether target or non-target) showing a reduction in the short axis to <10 mm. Tumor marker results were required to have normalized. PR was defined as a decrease of at least 30% in the sum of the diameters of target lesions, using baseline diameters as the reference. APD: All randomized participants who received at least 1 dose of study drug.

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

End point timeframe:

Randomization until measured progressive disease (Up To 23 Months)

|                                   |                                                    |                                   |  |  |
|-----------------------------------|----------------------------------------------------|-----------------------------------|--|--|
| <b>End point values</b>           | Ramucirumab +<br>Cyclophosphamide +<br>Vinorelbine | Cyclophosphamide +<br>Vinorelbine |  |  |
| Subject group type                | Reporting group                                    | Reporting group                   |  |  |
| Number of subjects analysed       | 20                                                 | 10                                |  |  |
| Units: Percentage of participants |                                                    |                                   |  |  |
| number (confidence interval 80%)  | 10 (2.7 to 24.5)                                   | 10 (1.1 to 33.7)                  |  |  |

### **Statistical analyses**

**Secondary: Duration of Response (DoR)**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                            |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Duration of Response (DoR) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                            |
| DoR is defined as the time from the date that measurement criteria for CR or PR (whichever is first recorded) are first met until the first date that disease is recurrent or objective disease progression is observed, per RECIST 1.1 criteria, or the date of death from any cause in the absence of documented disease progression or recurrence. Participants known to be alive and without disease progression were censored at the date of their last adequate tumor assessment per RECIST 1.1 criteria, or date of randomization (whichever is later). APD: All randomized participants who received at least 1 dose of study drug and who had CR or PR responses (including the censored participants). Number of participants censored in Ramucirumab + Cyclophosphamide + Vinorelbine = 0, Cyclophosphamide + Vinorelbine = 1. |                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Secondary                  |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                            |
| Date of CR or PR to Date of Objective Disease Progression or Death Due to Any Cause (Up To 23 Months)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                            |

| End point values                 | Ramucirumab + Cyclophosphamide + Vinorelbine | Cyclophosphamide + Vinorelbine |  |  |
|----------------------------------|----------------------------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group                              | Reporting group                |  |  |
| Number of subjects analysed      | 2 <sup>[4]</sup>                             | 1 <sup>[5]</sup>               |  |  |
| Units: Months                    |                                              |                                |  |  |
| median (confidence interval 80%) | 9.55 (4.89 to 9999)                          | 9999 (9999 to 9999)            |  |  |

Notes:

[4] - 9999=N/A= There were not enough events to estimate the upper limit of the 80% confidence interval.

[5] - 9999=N/A=DoR couldn't be calculated as the participant did not achieve the event and was censored.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Complete Response (CR) : Percentage of Participants Who Achieved a CR**

|                                                                                                                                                                                                                                                                                                                                                                                             |                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                             | Complete Response (CR) : Percentage of Participants Who Achieved a CR |
| End point description:                                                                                                                                                                                                                                                                                                                                                                      |                                                                       |
| CR was defined as the disappearance of all target lesions, with any pathological lymph nodes (whether target or non-target) showing a reduction in the short axis to <10 mm. Tumor marker results were required to have normalized. All randomized participants who received at least one dose of study drug. APD:All randomized participants who received at least one dose of study drug. |                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                                                                              | Secondary                                                             |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                        |                                                                       |
| Randomization until measured progressive disease (Up To 23 Months)                                                                                                                                                                                                                                                                                                                          |                                                                       |

| End point values                  | Ramucirumab + Cyclophosphamide + Vinorelbine | Cyclophosphamide + Vinorelbine |  |  |
|-----------------------------------|----------------------------------------------|--------------------------------|--|--|
| Subject group type                | Reporting group                              | Reporting group                |  |  |
| Number of subjects analysed       | 20                                           | 10                             |  |  |
| Units: Percentage of participants |                                              |                                |  |  |
| number (confidence interval 80%)  | 5.0 (0.5 to 18.1)                            | 0 (0.0 to 20.6)                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics (PK): Maximum Serum Concentration of Ramucirumab (Cmax)

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Pharmacokinetics (PK): Maximum Serum Concentration of Ramucirumab (Cmax) <sup>[6]</sup> |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

Cmax was the concentration of study drug in the blood after the dose is administered. It was measured post-dose and was summarized using descriptive statistics. APD: All randomized participants who received at least one dose of Ramucirumab and had evaluable PK data for this outcome.

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

End point timeframe:

End of ramucirumab infusion on Day 1 of Cycle 1

Notes:

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

Justification: This outcome is planned for Ramucirumab arm only.

| End point values                                    | Ramucirumab + Cyclophosphamide + Vinorelbine |  |  |  |
|-----------------------------------------------------|----------------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                              |  |  |  |
| Number of subjects analysed                         | 14                                           |  |  |  |
| Units: microgram per milliliter (µg/mL)             |                                              |  |  |  |
| geometric mean (geometric coefficient of variation) | 238 (± 35)                                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK: Minimum Serum Concentration of Ramucirumab (Cmin)

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | PK: Minimum Serum Concentration of Ramucirumab (Cmin) <sup>[7]</sup> |
|-----------------|----------------------------------------------------------------------|

End point description:

Cmin was the concentration of study drug in the blood immediately before the next dose was administered. It was measured pre-dose at all visits and was summarized using descriptive statistics. APD: All randomized participants who received at least one dose of Ramucirumab and had evaluable PK

data for this outcome. Number analyzed refers to participants evaluable at specified time points.

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

End point timeframe:

Prior to ramucirumab infusion on - Day 15 of Cycle 1 and Day 1 of Cycles 2, 4, 7, and 10

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome is planned for Ramucirumab arm only.

|                                                     |                                                       |  |  |  |
|-----------------------------------------------------|-------------------------------------------------------|--|--|--|
| <b>End point values</b>                             | Ramucirumab<br>+<br>Cyclophosphamide +<br>Vinorelbine |  |  |  |
| Subject group type                                  | Reporting group                                       |  |  |  |
| Number of subjects analysed                         | 13 <sup>[8]</sup>                                     |  |  |  |
| Units: microgram per milliliter (µg/mL)             |                                                       |  |  |  |
| geometric mean (geometric coefficient of variation) |                                                       |  |  |  |
| Day 15 of Cycle 1, Number Analyzed = 13             | 41.6 (± 57)                                           |  |  |  |
| Day 1 of Cycle 2 , Number Analyzed = 9              | 88.7 (± 47)                                           |  |  |  |
| Day 1 of Cycle 4 , Number Analyzed = 7              | 157 (± 37)                                            |  |  |  |
| Day 1 of Cycle 7 , Number Analyzed = 4              | 155 (± 28)                                            |  |  |  |
| Day 1 of Cycle 10 , Number Analyzed = 2             | 9999 (± 9999)                                         |  |  |  |

Notes:

[8] - 9999=N/A due to insufficient participants. Individual values reported: 151 µg/mL, 207 µg/mL.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment-Emergent Anti-Drug Antibodies (TE-ADA)

|                 |                                                                              |
|-----------------|------------------------------------------------------------------------------|
| End point title | Number of Participants With Treatment-Emergent Anti-Drug Antibodies (TE-ADA) |
|-----------------|------------------------------------------------------------------------------|

End point description:

A TE-ADA evaluable participant is considered TE-ADA positive if they have at least one post-baseline ADA titer that is a 4-fold or greater increase from their baseline titer (treatment-boosted); alternatively, if the baseline ADA result is Not Present, the participant is considered TE-ADA positive if there is at least one post-baseline ADA result that is Present with a titer greater than or equal to 1:20 (treatment-induced). APD: All randomized participants who received at least one dose of study drug and had at least one non-missing baseline, post baseline ADA value.

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

End point timeframe:

Baseline Up to 23 months

|                             |                                                       |                                   |  |  |
|-----------------------------|-------------------------------------------------------|-----------------------------------|--|--|
| <b>End point values</b>     | Ramucirumab<br>+<br>Cyclophosphamide +<br>Vinorelbine | Cyclophosphamide +<br>Vinorelbine |  |  |
| Subject group type          | Reporting group                                       | Reporting group                   |  |  |
| Number of subjects analysed | 13                                                    | 5                                 |  |  |
| Units: participants         | 0                                                     | 0                                 |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline Up to 44.33 months

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. Based on the planned safety analysis, adverse events were collected and reported by treatment regimen.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 29.0   |

### Reporting groups

|                       |                                              |
|-----------------------|----------------------------------------------|
| Reporting group title | Ramucirumab + Cyclophosphamide + Vinorelbine |
|-----------------------|----------------------------------------------|

Reporting group description:

Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

- Ramucirumab administered intravenously at a dose of 12 mg/kg as a one-hour infusion on days 1 and 15.
- Cyclophosphamide administered orally at 25 mg/m<sup>2</sup> daily from days 1 to 28.
- Vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Cyclophosphamide + Vinorelbine |
|-----------------------|--------------------------------|

Reporting group description:

Participants received the following treatments in a 28-day cycle, continuing until disease progression or a criterion for discontinuation was met.

- Cyclophosphamide administered orally at 25 mg/m<sup>2</sup> daily from days 1 to 28.
- Vinorelbine administered intravenously at 25 mg/m<sup>2</sup> on days 1, 8, and 15.

| Serious adverse events                            | Ramucirumab +<br>Cyclophosphamide<br>+ Vinorelbine | Cyclophosphamide +<br>Vinorelbine |  |
|---------------------------------------------------|----------------------------------------------------|-----------------------------------|--|
| Total subjects affected by serious adverse events |                                                    |                                   |  |
| subjects affected / exposed                       | 6 / 20 (30.00%)                                    | 3 / 10 (30.00%)                   |  |
| number of deaths (all causes)                     | 12                                                 | 7                                 |  |
| number of deaths resulting from adverse events    |                                                    |                                   |  |
| Injury, poisoning and procedural complications    |                                                    |                                   |  |
| post procedural haemorrhage                       |                                                    |                                   |  |
| alternative dictionary used:<br>MedDRA 29.0       |                                                    |                                   |  |
| subjects affected / exposed                       | 1 / 20 (5.00%)                                     | 0 / 10 (0.00%)                    |  |
| occurrences causally related to treatment / all   | 1 / 1                                              | 0 / 0                             |  |
| deaths causally related to treatment / all        | 0 / 0                                              | 0 / 0                             |  |
| vascular access complication                      |                                                    |                                   |  |
| alternative dictionary used:<br>MedDRA 29.0       |                                                    |                                   |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                             |                 |                 |  |
| syncope                                              |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |
| subjects affected / exposed                          | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| chest pain                                           |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| pyrexia                                              |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |
| subjects affected / exposed                          | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders                 |                 |                 |  |
| febrile neutropenia                                  |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |
| subjects affected / exposed                          | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all      | 2 / 3           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                           |                 |                 |  |
| ascites                                              |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| nausea                                               |                 |                 |  |
| alternative dictionary used: MedDRA 29.0             |                 |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| small intestinal obstruction                    |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Renal and urinary disorders                     |                |                 |  |
| acute kidney injury                             |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Infections and infestations                     |                |                 |  |
| bacteraemia                                     |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| device related infection                        |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| cystitis                                        |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| cellulitis                                      |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 10 (10.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| influenza                                       |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| viral diarrhoea                                 |                |                 |  |
| alternative dictionary used: MedDRA 29.0        |                |                 |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                   | Ramucirumab +<br>Cyclophosphamide<br>+ Vinorelbine | Cyclophosphamide +<br>Vinorelbine |  |
|---------------------------------------------------------------------|----------------------------------------------------|-----------------------------------|--|
| Total subjects affected by non-serious adverse events               |                                                    |                                   |  |
| subjects affected / exposed                                         | 20 / 20 (100.00%)                                  | 10 / 10 (100.00%)                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                    |                                   |  |
| tumour pain                                                         |                                                    |                                   |  |
| alternative dictionary used: MedDRA 29.0                            |                                                    |                                   |  |
| subjects affected / exposed                                         | 1 / 20 (5.00%)                                     | 0 / 10 (0.00%)                    |  |
| occurrences (all)                                                   | 1                                                  | 0                                 |  |
| Vascular disorders                                                  |                                                    |                                   |  |
| hypertension                                                        |                                                    |                                   |  |
| alternative dictionary used: MedDRA 29.0                            |                                                    |                                   |  |
| subjects affected / exposed                                         | 3 / 20 (15.00%)                                    | 0 / 10 (0.00%)                    |  |
| occurrences (all)                                                   | 3                                                  | 0                                 |  |
| phlebitis                                                           |                                                    |                                   |  |
| alternative dictionary used: MedDRA 29.0                            |                                                    |                                   |  |
| subjects affected / exposed                                         | 1 / 20 (5.00%)                                     | 0 / 10 (0.00%)                    |  |
| occurrences (all)                                                   | 1                                                  | 0                                 |  |

|                                                                                                                                |                      |                      |  |
|--------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| superficial vein thrombosis<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 0 / 10 (0.00%)<br>0  |  |
| thrombosis<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 20 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |  |
| General disorders and administration<br>site conditions                                                                        |                      |                      |  |
| asthenia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 20 (10.00%)<br>2 | 2 / 10 (20.00%)<br>4 |  |
| chills<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 20 (10.00%)<br>2 | 0 / 10 (0.00%)<br>0  |  |
| catheter site rash<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)          | 0 / 20 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |  |
| early satiety<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)               | 1 / 20 (5.00%)<br>1  | 0 / 10 (0.00%)<br>0  |  |
| fatigue<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                     | 5 / 20 (25.00%)<br>6 | 2 / 10 (20.00%)<br>3 |  |
| impaired healing<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)            | 1 / 20 (5.00%)<br>1  | 0 / 10 (0.00%)<br>0  |  |
| mucosal inflammation<br>alternative dictionary used:                                                                           |                      |                      |  |

|                                             |                 |                 |  |
|---------------------------------------------|-----------------|-----------------|--|
| MedDRA 29.0                                 |                 |                 |  |
| subjects affected / exposed                 | 4 / 20 (20.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                           | 4               | 0               |  |
| malaise                                     |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                           | 0               | 1               |  |
| localised oedema                            |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |  |
| occurrences (all)                           | 1               | 0               |  |
| non-cardiac chest pain                      |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                           | 0               | 1               |  |
| pain                                        |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |  |
| occurrences (all)                           | 1               | 0               |  |
| pyrexia                                     |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 5 / 20 (25.00%) | 4 / 10 (40.00%) |  |
| occurrences (all)                           | 7               | 7               |  |
| thirst                                      |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                           | 0               | 1               |  |
| Immune system disorders                     |                 |                 |  |
| anaphylactic reaction                       |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                           | 0               | 1               |  |
| seasonal allergy                            |                 |                 |  |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                |                                                                                                                               |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>type iv hypersensitivity reaction</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>1 / 20 (5.00%)</p> <p>2</p> <p>1 / 20 (5.00%)</p> <p>1</p>                                                                                                  | <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                                                 |  |
| <p>Reproductive system and breast disorders</p> <p>vaginal discharge</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed<sup>[1]</sup></p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>1 / 5 (20.00%)</p> <p>1</p>                                                                                                                                 | <p>0 / 10 (0.00%)</p> <p>0</p>                                                                                                |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspnoea</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>epistaxis</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasal congestion</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>oropharyngeal pain</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rhinitis allergic</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> | <p>6 / 20 (30.00%)</p> <p>6</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>8 / 20 (40.00%)</p> <p>11</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>2 / 20 (10.00%)</p> <p>2</p> | <p>1 / 10 (10.00%)</p> <p>3</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>2 / 10 (20.00%)</p> <p>2</p> |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                  |                                                                                                 |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tachypnoea</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                     | <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 20 (0.00%)</p> <p>0</p>                                    | <p>0 / 10 (0.00%)</p> <p>0</p> <p>1 / 10 (10.00%)</p> <p>1</p>                                  |  |
| <p>Psychiatric disorders</p> <p>confusional state</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>insomnia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                             | <p>1 / 20 (5.00%)</p> <p>1</p> <p>1 / 20 (5.00%)</p> <p>1</p>                                    | <p>0 / 10 (0.00%)</p> <p>0</p> <p>1 / 10 (10.00%)</p> <p>1</p>                                  |  |
| <p>Product issues</p> <p>device dislocation</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                   | <p>1 / 20 (5.00%)</p> <p>1</p>                                                                   | <p>0 / 10 (0.00%)</p> <p>0</p>                                                                  |  |
| <p>Investigations</p> <p>alanine aminotransferase increased</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>activated partial thromboplastin time prolonged</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>anion gap decreased</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>aspartate aminotransferase increased</p> <p>alternative dictionary used:</p> | <p>10 / 20 (50.00%)</p> <p>15</p> <p>3 / 20 (15.00%)</p> <p>3</p> <p>1 / 20 (5.00%)</p> <p>1</p> | <p>2 / 10 (20.00%)</p> <p>15</p> <p>1 / 10 (10.00%)</p> <p>2</p> <p>0 / 10 (0.00%)</p> <p>0</p> |  |

|                                             |                 |                 |
|---------------------------------------------|-----------------|-----------------|
| MedDRA 29.0                                 |                 |                 |
| subjects affected / exposed                 | 7 / 20 (35.00%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 11              | 17              |
| blood lactate dehydrogenase increased       |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 2               | 0               |
| blood bilirubin increased                   |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 2               | 0               |
| blood chloride decreased                    |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 1               |
| blood creatine increased                    |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 2               | 0               |
| blood creatinine increased                  |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 3 / 20 (15.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 11              | 0               |
| blood alkaline phosphatase increased        |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 4 / 20 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all)                           | 6               | 1               |
| blood urea increased                        |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 6               | 0               |
| blood thyroid stimulating hormone increased |                 |                 |
| alternative dictionary used: MedDRA 29.0    |                 |                 |

|                                          |                  |                 |
|------------------------------------------|------------------|-----------------|
| subjects affected / exposed              | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                        | 1                | 0               |
| gamma-glutamyltransferase increased      |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 2 / 20 (10.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 2                | 0               |
| glomerular filtration rate decreased     |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                        | 1                | 0               |
| haemoglobin increased                    |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                        | 1                | 0               |
| international normalised ratio increased |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 2 / 20 (10.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 2                | 0               |
| lymphocyte count decreased               |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 5 / 20 (25.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                        | 7                | 18              |
| neutrophil count decreased               |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 10 / 20 (50.00%) | 5 / 10 (50.00%) |
| occurrences (all)                        | 33               | 26              |
| platelet count decreased                 |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |
| subjects affected / exposed              | 3 / 20 (15.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                        | 14               | 2               |
| weight increased                         |                  |                 |
| alternative dictionary used: MedDRA 29.0 |                  |                 |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                 |                                                                                                 |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>weight decreased</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>white blood cell count decreased</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                         | <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 20 (0.00%)</p> <p>0</p> <p>11 / 20 (55.00%)</p> <p>39</p> | <p>0 / 10 (0.00%)</p> <p>0</p> <p>2 / 10 (20.00%)</p> <p>2</p> <p>6 / 10 (60.00%)</p> <p>34</p> |  |
| <p>Injury, poisoning and procedural complications</p> <p>infusion related reaction</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>limb injury</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>wound complication</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 20 (5.00%)</p> <p>1</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>1 / 20 (5.00%)</p> <p>1</p>    | <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>    |  |
| <p>Cardiac disorders</p> <p>angina pectoris</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>sinus tachycardia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tachycardia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p>                                                                                                     | <p>1 / 20 (5.00%)</p> <p>1</p> <p>2 / 20 (10.00%)</p> <p>2</p>                                  | <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                   |  |

|                                                                                                                                  |                        |                       |  |
|----------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                 | 1 / 20 (5.00%)<br>1    | 1 / 10 (10.00%)<br>1  |  |
| Nervous system disorders                                                                                                         |                        |                       |  |
| cerebrovascular accident<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)      | 0 / 20 (0.00%)<br>0    | 1 / 10 (10.00%)<br>1  |  |
| dizziness<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 20 (5.00%)<br>1    | 2 / 10 (20.00%)<br>2  |  |
| dysgeusia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 20 (5.00%)<br>1    | 0 / 10 (0.00%)<br>0   |  |
| headache<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                      | 10 / 20 (50.00%)<br>17 | 1 / 10 (10.00%)<br>1  |  |
| neuropathy peripheral<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)         | 1 / 20 (5.00%)<br>1    | 0 / 10 (0.00%)<br>0   |  |
| peripheral sensory neuropathy<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1    | 0 / 10 (0.00%)<br>0   |  |
| Blood and lymphatic system disorders                                                                                             |                        |                       |  |
| anaemia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                       | 8 / 20 (40.00%)<br>13  | 2 / 10 (20.00%)<br>19 |  |
| febrile neutropenia<br>alternative dictionary used:<br>MedDRA 29.0                                                               |                        |                       |  |

|                                                                                                                                                                                                                                               |  |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                                                                                                     |  |  |  |
| <p>lymphopenia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                              |  |  |  |
| <p>leukopenia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 20 (10.00%)</p> <p>3</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                              |  |  |  |
| <p>neutropenia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>11 / 20 (55.00%)</p> <p>28</p> <p>1 / 10 (10.00%)</p> <p>3</p>                                          |  |  |  |
| <p>thrombocytopenia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>3 / 20 (15.00%)</p> <p>3</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                        |  |  |  |
| <p>Eye disorders</p> <p>eye swelling</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p>                        |  |  |  |
| <p>ocular hyperaemia</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p>                                        |  |  |  |
| <p>Gastrointestinal disorders</p> <p>abdominal distension</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 20 (10.00%)</p> <p>2</p> <p>3 / 10 (30.00%)</p> <p>4</p> |  |  |  |
| <p>abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p>                                                                                                                                                                     |  |  |  |

|                                             |                  |                 |
|---------------------------------------------|------------------|-----------------|
| subjects affected / exposed                 | 11 / 20 (55.00%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 18               | 2               |
| anorectal discomfort                        |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1                | 0               |
| ascites                                     |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 2                | 0               |
| constipation                                |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 7 / 20 (35.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                           | 7                | 3               |
| dyspepsia                                   |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1                | 0               |
| dry mouth                                   |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)   | 1 / 10 (10.00%) |
| occurrences (all)                           | 0                | 1               |
| diarrhoea                                   |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 7 / 20 (35.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                           | 12               | 2               |
| eructation                                  |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)   | 1 / 10 (10.00%) |
| occurrences (all)                           | 0                | 1               |
| flatulence                                  |                  |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                  |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1                | 0               |

|                                                                                                                      |                       |                      |  |
|----------------------------------------------------------------------------------------------------------------------|-----------------------|----------------------|--|
| gastritis<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)         | 2 / 20 (10.00%)<br>3  | 0 / 10 (0.00%)<br>0  |  |
| gingival bleeding<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1   | 0 / 10 (0.00%)<br>0  |  |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)      | 1 / 20 (5.00%)<br>2   | 0 / 10 (0.00%)<br>0  |  |
| gingival pain<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)     | 1 / 20 (5.00%)<br>3   | 0 / 10 (0.00%)<br>0  |  |
| nausea<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)            | 4 / 20 (20.00%)<br>6  | 3 / 10 (30.00%)<br>7 |  |
| stomatitis<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)        | 3 / 20 (15.00%)<br>4  | 0 / 10 (0.00%)<br>0  |  |
| vomiting<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)          | 6 / 20 (30.00%)<br>11 | 4 / 10 (40.00%)<br>4 |  |
| Skin and subcutaneous tissue disorders                                                                               |                       |                      |  |
| dry skin<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)          | 1 / 20 (5.00%)<br>1   | 0 / 10 (0.00%)<br>0  |  |
| eczema<br>alternative dictionary used:<br>MedDRA 29.0                                                                |                       |                      |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                               |                                                                                                                                |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>petechiae</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>skin ulcer</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                               | <p>2 / 20 (10.00%)</p> <p>5</p> <p>2 / 20 (10.00%)</p> <p>2</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>0 / 20 (0.00%)</p> <p>0</p> | <p>1 / 10 (10.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>0 / 10 (0.00%)</p> <p>0</p> <p>1 / 10 (10.00%)</p> <p>1</p>  |  |
| <p>Renal and urinary disorders</p> <p>dysuria</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>haematuria</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>micturition urgency</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>proteinuria</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pollakiuria</p> <p>alternative dictionary used:<br/>MedDRA 29.0</p> | <p>0 / 20 (0.00%)</p> <p>0</p> <p>0 / 20 (0.00%)</p> <p>0</p> <p>0 / 20 (0.00%)</p> <p>0</p> <p>9 / 20 (45.00%)</p> <p>14</p> | <p>2 / 10 (20.00%)</p> <p>2</p> <p>1 / 10 (10.00%)</p> <p>1</p> <p>1 / 10 (10.00%)</p> <p>1</p> <p>0 / 10 (0.00%)</p> <p>0</p> |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                   |                                                                                                                                    |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1 / 20 (5.00%)<br>2                                                                                                               | 1 / 10 (10.00%)<br>1                                                                                                               |  |
| Endocrine disorders<br>hypothyroidism<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 2 / 20 (10.00%)<br>2                                                                                                              | 0 / 10 (0.00%)<br>0                                                                                                                |  |
| Musculoskeletal and connective tissue disorders<br>arthralgia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)<br><br>back pain<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)<br><br>myalgia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)<br><br>muscular weakness<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)<br><br>pain in extremity<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1<br><br>7 / 20 (35.00%)<br>7<br><br>2 / 20 (10.00%)<br>2<br><br>1 / 20 (5.00%)<br>1<br><br>1 / 20 (5.00%)<br>2 | 0 / 10 (0.00%)<br>0<br><br>2 / 10 (20.00%)<br>3<br><br>1 / 10 (10.00%)<br>1<br><br>0 / 10 (0.00%)<br>0<br><br>1 / 10 (10.00%)<br>1 |  |
| Infections and infestations<br>cellulitis<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)<br><br>covid-19<br>alternative dictionary used:<br>MedDRA 29.0                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0 / 20 (0.00%)<br>0                                                                                                               | 1 / 10 (10.00%)<br>2                                                                                                               |  |

|                                             |                 |                 |
|---------------------------------------------|-----------------|-----------------|
| subjects affected / exposed                 | 3 / 20 (15.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 3               | 0               |
| cystitis                                    |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               |
| ear lobe infection                          |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               |
| gingivitis                                  |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 2               | 0               |
| klebsiella infection                        |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               |
| oral herpes                                 |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 1               |
| nasopharyngitis                             |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                           | 1               | 2               |
| skin infection                              |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 3               | 0               |
| upper respiratory tract infection           |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 1               |

|                                                                                                                                                      |                      |                      |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 20 (10.00%)<br>2 | 1 / 10 (10.00%)<br>1 |  |
| wound infection<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 20 (5.00%)<br>3  | 0 / 10 (0.00%)<br>0  |  |
| Metabolism and nutrition disorders<br>dehydration<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 1 / 10 (10.00%)<br>1 |  |
| decreased appetite<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                | 2 / 20 (10.00%)<br>2 | 3 / 10 (30.00%)<br>3 |  |
| hypercalcaemia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                    | 2 / 20 (10.00%)<br>2 | 0 / 10 (0.00%)<br>0  |  |
| hyperglycaemia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 20 (5.00%)<br>1  | 1 / 10 (10.00%)<br>1 |  |
| hyperkalaemia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                     | 2 / 20 (10.00%)<br>3 | 0 / 10 (0.00%)<br>0  |  |
| hypermagnesaemia<br>alternative dictionary used:<br>MedDRA 29.0<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 20 (5.00%)<br>2  | 0 / 10 (0.00%)<br>0  |  |
| hypernatraemia<br>alternative dictionary used:<br>MedDRA 29.0                                                                                        |                      |                      |  |

|                                             |                 |                 |
|---------------------------------------------|-----------------|-----------------|
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               |
| hyperphosphataemia                          |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 7               | 2               |
| hypertriglyceridaemia                       |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 1 / 20 (5.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               |
| hypoalbuminaemia                            |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 3 / 20 (15.00%) | 1 / 10 (10.00%) |
| occurrences (all)                           | 7               | 2               |
| hypocalcaemia                               |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 3 / 20 (15.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 12              | 0               |
| hypoglycaemia                               |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                           | 3               | 0               |
| hypokalaemia                                |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 2 / 20 (10.00%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 2               | 4               |
| hyponatraemia                               |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 5 / 20 (25.00%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 7               | 3               |
| hypophosphataemia                           |                 |                 |
| alternative dictionary used:<br>MedDRA 29.0 |                 |                 |
| subjects affected / exposed                 | 0 / 20 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 1               |

|                                             |                |                |  |
|---------------------------------------------|----------------|----------------|--|
| hypomagnesaemia                             |                |                |  |
| alternative dictionary used:<br>MedDRA 29.0 |                |                |  |
| subjects affected / exposed                 | 1 / 20 (5.00%) | 0 / 10 (0.00%) |  |
| occurrences (all)                           | 3              | 0              |  |

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Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in female participants have had the number of participants "At Risk" adjusted accordingly.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported