



Clinical trial results:

A Phase I Study of Monotherapy Dalotuzumab and Ridaforolimus-Dalotuzumab Combination Treatment in Paediatric Patients with Advanced Solid Tumours

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2011-003407-38 |
| Trial protocol | GB FR |
| Global end of trial date | 25 September 2013 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 26 February 2016 |
| First version publication date | 13 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 8669-062 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01431547 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill RD, Kenilworth NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 September 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 September 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 September 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

This is a study of dalotuzumab given as monotherapy and in combination with ridaforolimus for pediatric participants with advanced solid tumors. This study will find the maximum tolerated dose (MTD) and collect pharmacokinetic (PK) data for dalotuzumab alone and in combination with ridaforolimus.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 21 February 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 7 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | France: 11 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 17 |

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) | 12 |
| Adolescents (12-17 years) | 12 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants from age 3 to <18 years were enrolled in the dalotuzumab dose-finding cohorts; subjects of age 6 to <18 years could receive dalotuzumab-ridaforolimus combination therapy.

Period 1

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

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Dalotuzumab 900 mg/m ² |

Arm description:

Participants receive dalotuzumab 900 mg/m², intravenously (IV) every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

| | |
|------------------|------------------------------------|
| Arm title | Dalotuzumab 1200 mg/m ² |
|------------------|------------------------------------|

Arm description:

Participants receive dalotuzumab 1200 mg/m², IV, every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

| | |
|------------------|------------------------------------|
| Arm title | Dalotuzumab 1500 mg/m ² |
|------------------|------------------------------------|

Arm description:

Participants receive dalotuzumab 1500 mg/m², IV, every 3 weeks

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

Dosage and administration details:

Dalotuzumab at assigned dose (based on body surface area), intravenously

| | |
|---|--|
| Arm title | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
| Arm description: | |
| Participants receive dalotuzumab 900 mg/m ² , IV, every 3 weeks, plus ridaforolimus 28 mg/m ² enteric-coated tablets, orally, once per day for 5 days each week | |
| Arm type | Experimental |
| Investigational medicinal product name | dalotuzumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Dalotuzumab at assigned dose (based on body surface area), intravenously | |
| Investigational medicinal product name | ridaforolimus |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Ridaforolimus, enteric coated tablets. orally, once a day for 5 days per week | |

| Number of subjects in period 1 | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² |
|---------------------------------------|-----------------------------------|------------------------------------|------------------------------------|
| Started | 11 | 3 | 6 |
| Completed | 0 | 0 | 0 |
| Not completed | 11 | 3 | 6 |
| Physician decision | - | - | - |
| Consent withdrawn by subject | - | - | - |
| Adverse event, non-fatal | 1 | - | - |
| Lack of efficacy | 10 | 3 | 6 |

| Number of subjects in period 1 | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
|---------------------------------------|--|
| Started | 4 |
| Completed | 0 |
| Not completed | 4 |
| Physician decision | 1 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | - |
| Lack of efficacy | 2 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Dalotuzumab 900 mg/m ² |
| Reporting group description: | |
| Participants receive dalotuzumab 900 mg/m ² , intravenously (IV) every 3 weeks | |
| Reporting group title | Dalotuzumab 1200 mg/m ² |
| Reporting group description: | |
| Participants receive dalotuzumab 1200 mg/m ² , IV, every 3 weeks | |
| Reporting group title | Dalotuzumab 1500 mg/m ² |
| Reporting group description: | |
| Participants receive dalotuzumab 1500 mg/m ² , IV, every 3 weeks | |
| Reporting group title | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
| Reporting group description: | |
| Participants receive dalotuzumab 900 mg/m ² , IV, every 3 weeks, plus ridaforolimus 28 mg/m ² enteric-coated tablets, orally, once per day for 5 days each week | |

| Reporting group values | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² |
|--|-----------------------------------|------------------------------------|------------------------------------|
| Number of subjects | 11 | 3 | 6 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 6 | 1 | 4 |
| Adolescents (12-17 years) | 5 | 2 | 2 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 1 | 4 |
| Male | 6 | 2 | 2 |

| Reporting group values | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² | Total | |
|--|--|-------|--|
| Number of subjects | 4 | 24 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 1 | 12 | |

| | | | |
|---------------------------|---|----|--|
| Adolescents (12-17 years) | 3 | 12 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 12 | |
| Male | 2 | 12 | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Dalotuzumab 900 mg/m ² |
| Reporting group description: Participants receive dalotuzumab 900 mg/m ² , intravenously (IV) every 3 weeks | |
| Reporting group title | Dalotuzumab 1200 mg/m ² |
| Reporting group description: Participants receive dalotuzumab 1200 mg/m ² , IV, every 3 weeks | |
| Reporting group title | Dalotuzumab 1500 mg/m ² |
| Reporting group description: Participants receive dalotuzumab 1500 mg/m ² , IV, every 3 weeks | |
| Reporting group title | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
| Reporting group description: Participants receive dalotuzumab 900 mg/m ² , IV, every 3 weeks, plus ridaforolimus 28 mg/m ² enteric-coated tablets, orally, once per day for 5 days each week | |

Primary: Number of Participants with Dose-limiting Toxicities (DLTs)

| | |
|---|--|
| End point title | Number of Participants with Dose-limiting Toxicities (DLTs) ^[1] |
| End point description: A dose-limiting toxicity is an event (medical or clinical) that results in a change in the study drug dose. | |
| End point type | Primary |
| End point timeframe: Up to 21 days (Cycle 1) | |

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

| End point values | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
|-----------------------------|-----------------------------------|------------------------------------|------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 3 | 6 | 4 |
| Units: Participants | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve from Hour 0 to Infinity (AUC_{0-inf}) for Dalotuzumab Alone or in Combination with Ridaforolimus

| | |
|-----------------|---|
| End point title | Area Under the Concentration-Time Curve from Hour 0 to Infinity (AUC _{0-inf}) for Dalotuzumab Alone or in Combination with Ridaforolimus ^[2] |
|-----------------|---|

End point description:

AUC is a measure of the amount of drug in the body over time. The geometric mean provides the

typical value of this set of numbers by using the product of their values; the coefficient of variation provides the percent of the geometric means represented by the standard deviation and is used to compensate for the inherent differences among participants in the study.

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

End point timeframe:

Pre-dose and at 1, 24, 48, 168 (Day 8), and 336 hours (Day 15) post first infusion; pre-dose at Week 4 (Day 22), Week 7 (Day 43), and Weeks 13 and 19.

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

| End point values | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
|---|--------------------------------------|---------------------------------------|---------------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 ^[3] | 3 ^[4] | 6 ^[5] | 4 ^[6] |
| Units: hr*ug/mL | | | | |
| geometric mean (geometric coefficient of variation) | 87900 (± 61.2) | 164000 (± 106) | 186000 (± 79.2) | 80300 (± 24.5) |

Notes:

[3] - All participants taking ≥1 dose of study drug(s) having required samples taken and analyzed

[4] - All participants taking ≥1 dose of study drug(s) having required samples taken and analyzed

[5] - All participants taking ≥1 dose of study drug(s) having required samples taken and analyzed

[6] - All participants taking ≥1 dose of study drug(s) having required samples taken and analyzed

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve from Hour 0 to Hour 24 (AUC0-24) for Ridaforolimus in Combination with Dalotuzumab

| | |
|-----------------|--|
| End point title | Area Under the Concentration-Time Curve from Hour 0 to Hour 24 (AUC0-24) for Ridaforolimus in Combination with Dalotuzumab ^[7] ^[8] |
|-----------------|--|

End point description:

AUC 0-24 is a measure of the amount of drug in the body over 24 hours after the dose. The geometric mean provides the typical value for the group by using the product of the AUC0-24 values; the coefficient of variation provides the percent of the geometric mean represented by the standard deviation and is used to compensate for the inherent differences among participants in the group.

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

End point timeframe:

Pre-dose on Days 1-5 in the first cycle of therapy and post-dose on Day 5 at 0.5, 1, 2, 4, 8, 24, and 72 hours.

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

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

Justification: No statistical analysis was planned for this endpoint.

| | | | | |
|---|---|--|--|--|
| End point values | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 ^[9] | | | |
| Units: hr*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 2350 (± 38.5) | | | |

Notes:

[9] - One participant was excluded from the analysis due to limited samples

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for 30 days after the last dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Dalotuzumab 900 mg/m ² |
|-----------------------|-----------------------------------|

Reporting group description:

Participants receive dalotuzumab 900 mg/m², intravenously (IV) every 3 weeks

| | |
|-----------------------|------------------------------------|
| Reporting group title | Dalotuzumab 1200 mg/m ² |
|-----------------------|------------------------------------|

Reporting group description:

Participants receive dalotuzumab 1200 mg/m², IV, every 3 weeks

| | |
|-----------------------|------------------------------------|
| Reporting group title | Dalotuzumab 1500 mg/m ² |
|-----------------------|------------------------------------|

Reporting group description:

Participants receive dalotuzumab 1500 mg/m², IV, every 3 weeks

| | |
|-----------------------|--|
| Reporting group title | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² |
|-----------------------|--|

Reporting group description:

Participants receive dalotuzumab 900 mg/m², IV, every 3 weeks, plus ridaforolimus 28 mg/m² enteric-coated tablets, orally, once per day for 5 days each week

| Serious adverse events | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² |
|---|-----------------------------------|------------------------------------|------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 11 (63.64%) | 1 / 3 (33.33%) | 4 / 6 (66.67%) |
| number of deaths (all causes) | 3 | 1 | 1 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|-----------------|----------------|----------------|
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Neurological decompensation | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal chest pain | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--|--|--|
| Serious adverse events | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour pain | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Neurological decompensation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Dalotuzumab 900 mg/m ² | Dalotuzumab 1200 mg/m ² | Dalotuzumab 1500 mg/m ² |
|---|-----------------------------------|------------------------------------|------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 11 (100.00%) | 3 / 3 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| Tumour associated fever subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Tumour pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vascular disorders | | | |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Hot flush subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pallor subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vena cava thrombosis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Catheter site pain subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Chest pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Chills subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Fatigue subjects affected / exposed occurrences (all) | 4 / 11 (36.36%) 4 | 1 / 3 (33.33%) 1 | 3 / 6 (50.00%) 4 |
| General physical health deterioration | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 2 / 3 (66.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 6 | 3 | 3 |
| Soft tissue inflammation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Scrotal oedema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Orthopnoea | | | |

| | | | |
|--|----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pleural effusion subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Sneezing subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Tachypnoea subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Investigations Alanine aminotransferase decreased subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 2 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 4 | 0 / 3 (0.00%) 0 | 2 / 6 (33.33%) 2 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 3 |
| Bilirubin conjugated increased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood albumin decreased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|-------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Blood calcium decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood glucose decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gamma-glutamyltransferase | | | |

| | | | |
|------------------------------------|-----------------|----------------|----------------|
| increased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 5 | 0 | 1 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| High density lipoprotein increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Low density lipoprotein increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 | 1 |
| Platelet count decreased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Protein total decreased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 10 | 1 | 1 |

| | | | |
|--|-----------------|----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Head injury | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Scratch | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Cyanosis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Cerebellar syndrome | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 1 / 3 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 13 | 1 | 4 |

| | | | |
|--|----------------------|---------------------|---------------------|
| Hyperaesthesia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyporeflexia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 2 |
| Slow speech subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 5 | 1 / 3 (33.33%) 1 | 1 / 6 (16.67%) 1 |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Ear and labyrinth disorders | | | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Ear swelling subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 6 (0.00%) 0 |
| Otorrhoea subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 6 (0.00%) 0 |
| Eye disorders | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Diplopia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema of eyelid | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 4 | 1 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Ascites | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chapped lips | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 4 / 11 (36.36%) | 1 / 3 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 5 | 1 | 3 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyoaesthesia oral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 5 | 1 | 2 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vomiting | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 8 | 2 / 3 (66.67%) 2 | 3 / 6 (50.00%) 5 |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Palmar erythema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash papular | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 6 (0.00%) 0 |
| Rash pruritic subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Swelling face subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Renal and urinary disorders | | | |
| Cystitis noninfective subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 6 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Incontinence subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 3 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 4 | 0 / 3 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Bone pain | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 3 (66.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|-------------------------------------|-----------------|----------------|----------------|
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Sphingomonas paucimobilis infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 1 / 3 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 1 | 3 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 7 | 0 | 4 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hypernatraemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 10 | 0 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Hyponatraemia | | | |
| subjects affected / exposed | 4 / 11 (36.36%) | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 7 | 1 | 4 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 3 |

| | | | |
|---|--|--|--|
| Non-serious adverse events | Dalotuzumab 900 mg/m ² + ridaforolimus 28 mg/m ² | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tumour pain | | | |

| | | | |
|---|--------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pallor | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 3 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 3 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 3 | | |
| Soft tissue inflammation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Reproductive system and breast disorders Scrotal oedema subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 4 (75.00%) 4 | | |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Orthopnoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Pleural effusion | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Tachypnoea subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | | |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Investigations Alanine aminotransferase decreased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 3 / 4 (75.00%) 4 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 3 | | |
| Bilirubin conjugated increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Blood albumin decreased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Blood bilirubin increased | | | |

| | | | |
|-------------------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 5 | | |
| Blood calcium decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Blood glucose decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Blood potassium decreased | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | | |
| occurrences (all) | 4 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 4 | | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|----------------------|--|--|
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 4 | | |
| Haemoglobin increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| High density lipoprotein increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Low density lipoprotein increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 6 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 4 / 4 (100.00%) 8 | | |
| Protein total decreased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | | |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 2 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 3 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---------------------|--|--|
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Fall subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Head injury subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Scratch subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | | |
| Cardiac disorders Cyanosis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Tachycardia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 2 | | |
| Nervous system disorders Cerebellar syndrome subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 6 | | |
| Hyperaesthesia | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Hyporeflexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Slow speech | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |

| | | | |
|-----------------------------|----------------|--|--|
| Diplopia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema of eyelid | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Photophobia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Anal fissure | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Ascites | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| occurrences (all) | 8 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Hyoaesthesia oral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | | |
| occurrences (all) | 3 | | |
| Oral pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| occurrences (all) | 6 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 6 | | |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Palmar erythema | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Petechiae | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash macular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash papular | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Swelling face | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 5 | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | | |
| occurrences (all) | 4 | | |
| Bone pain | | | |

| | | | |
|-----------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 5 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 4 | | |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-------------------------------------|----------------|--|--|
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sphingomonas paucimobilis infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Cachexia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypernatraemia | | | |

| | | | |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported