

**Clinical trial results:****SAPROCAN: Saracatinib (AZD0530) and docetaxel in metastatic, castrate-refractory prostate cancer: a phase I/randomised phase II study by the UK NCRI Prostate Clinical Studies Group****Summary**

| | |
|--------------------------|------------------|
| EudraCT number | 2010-021447-41 |
| Trial protocol | GB |
| Global end of trial date | 31 December 2017 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 06 April 2022 |
| First version publication date | 21 August 2020 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Following publication of the final approved results on to the EudraCT database, whilst drafting a manuscript for a peer-reviewed journal, an issue was identified with one patient's death data and the corresponding derived values for the survival endpoints. The necessary corrections were made and the analyses were re-run. The conclusions of the study remained the same. This update is a correction. |

Trial information**Trial identification**

| | |
|-----------------------|--------------|
| Sponsor protocol code | SAPROCAN2011 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|----------------|
| ISRCTN number | ISRCTN22566729 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | NHS Greater Glasgow and Clyde |
| Sponsor organisation address | Ward 11, Dykebar Hospital, Paisley, United Kingdom, PA2 7DE |
| Public contact | Carol Evans, Clinical Trials Unit, Beatson West of Scotland Cancer Centre, Glasgow G12 0YN, 0141 301 7189, carol.evans@glasgow.ac.uk |
| Scientific contact | Carol Evans, Clinical Trials Unit, Beatson West of Scotland Cancer Centre, Glasgow G12 0YN, 0141 301 7189, carol.evans@glasgow.ac.uk |
| Sponsor organisation name | University of Glasgow |
| Sponsor organisation address | Room 327 Wolfson Medical School Building, Glasgow, United Kingdom, G12 8QQ |
| Public contact | Carol Evans, Clinical Trials Unit, Beatson West of Scotland Cancer Centre, Glasgow G12 0YN, 0141 301 7189, carol.evans@glasgow.ac.uk |
| Scientific contact | Carol Evans, Clinical Trials Unit, Beatson West of Scotland Cancer Centre, Glasgow G12 0YN, 0141 301 7189, carol.evans@glasgow.ac.uk |

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 | 31 December 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

For the first part of the study (phase I), the primary objective is to find a safe and tolerable dose for saracatinib (AZD0530) given in combination with standard chemotherapy treatment (docetaxel and prednisolone) for patients with metastatic castrate-refractory prostate cancer.

For the second part of the study (phase II), the primary objective is to investigate whether we can improve the benefits of chemotherapy cancer treatment for patients with metastatic castrate-refractory prostate cancer by adding a new drug, saracatinib (AZD0530).

Protection of trial subjects:

Patients were required to attend for visits and investigations that were considered additional to standard of care. The number and type of visits and assessments were fully explained verbally and in a Patient Information Sheet which patients were given time to read and discuss with family and the research team prior to consent. All staff involved in delivering the study were fully GCP trained. In the dose escalation phase (Phase I), patients were reviewed weekly for Dose Limiting Toxicities, and a Safety Review Committee met at the completion of each dose cohort to review the patient details and confirm the escalation to the next dose level where appropriate. For the Phase II component of the study, patients were made aware that half of the participants would receive study drug and half would receive a placebo, but that the treatment assigned would be unknown to the patient and the study team unless emergency unblinding was required.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 12 March 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 152 |
| Worldwide total number of subjects | 152 |
| EEA total number of subjects | 152 |

Notes:

Subjects enrolled per age group

| | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 36 |
| From 65 to 84 years | 116 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Phase I opened to recruitment in March 2012. 10 patients were recruited into 3 cohorts; 9 were evaluable.

Phase II opened to recruitment in October 2013 and was closed to recruitment in March 2016; 142 patients were randomised.

Pre-assignment

Screening details:

Following consent, all patients underwent screening to determine eligibility, including confirmation of disease progression, physical exam, blood tests (including testosterone), review of prior treatment (prior cytotoxic chemotherapy excluded, washout of >30 days for other IMP required)

Period 1

| | |
|------------------------------|--------------------|
| Period 1 title | Phase I & Phase II |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Phase I Cohort 1 |

Arm description:

Saracatinib (AZD0530) 50mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),

Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),

Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.

Each cycle is 21 days.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 50mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles.

| | |
|------------------|------------------|
| Arm title | Phase I Cohort 2 |
|------------------|------------------|

Arm description:

Saracatinib (AZD0530) 125mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),

Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),

Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.

Each cycle is 21 days

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-------------|
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 125mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles.

| | |
|------------------|------------------|
| Arm title | Phase I Cohort 3 |
|------------------|------------------|

Arm description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles.

| | |
|------------------|-----------------|
| Arm title | Phase II Active |
|------------------|-----------------|

Arm description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression. Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|------------------|------------------|
| Arm title | Phase II Placebo |
|------------------|------------------|

Arm description:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days after 7 day run-in period with placebo.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression. Each cycle is 21 days after 7 day run-in period with placebo.

| Number of subjects in period 1 | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 |
|---------------------------------------|------------------|------------------|------------------|
| Started | 3 | 3 | 4 |
| Completed | 3 | 3 | 4 |

| Number of subjects in period 1 | Phase II Active | Phase II Placebo |
|---------------------------------------|-----------------|------------------|
| Started | 71 | 71 |
| Completed | 71 | 71 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Phase I |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Phase I Cohort 1 |

Arm description:

Saracatinib (AZD0530) 50mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression),
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days .

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 50mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles.

| | |
|---|------------------|
| Arm title | Phase I Cohort 2 |
| Arm description: Saracatinib (AZD0530) 125mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m2 intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days . | |
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: Saracatinib (AZD0530) 125mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles. | |

| | |
|---|------------------|
| Arm title | Phase I Cohort 3 |
| Arm description: Saracatinib (AZD0530) 175mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m2 intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days . | |
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: Saracatinib (AZD0530) 175mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression). After cycle 1, dispensed in 21 day cycles. | |

| | |
|--|-------------------------------------|
| Arm title | Phase II Patients |
| Arm description: Only required to overrule system error that requires the same number or fewer patients in a subsequent period: no summaries or analysis will be provided | |
| Arm type | Required only for issue with system |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 |
|--|------------------|------------------|------------------|
| Started | 3 | 3 | 4 |
| Completed | 3 | 3 | 3 |
| Not completed | 0 | 0 | 1 |
| Unevaluable (insufficient treatment taken) | - | - | 1 |

| Number of subjects in period 2 | Phase II Patients |
|--|-------------------|
| Started | 142 |
| Completed | 142 |
| Not completed | 0 |
| Unevaluable (insufficient treatment taken) | - |

Period 3

| | |
|------------------------------|-------------------------------------|
| Period 3 title | Phase II |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Data analyst |

Blinding implementation details:

Placebo-controlled. Packaging, labelling and preparation of the trial drug and placebo were performed in a way that ensured blinding throughout this part of the trial.

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Phase II Active |

Arm description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression, Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Saracatinib |
| Investigational medicinal product code | AZD0530 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression. Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|------------------|------------------|
| Arm title | Phase II Placebo |
|------------------|------------------|

Arm description:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression, Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days after 7 day run-in period with placebo.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression. Each cycle is 21 days after 7 day run-in period with placebo.

| Number of subjects in period 3 ^[1] | Phase II Active | Phase II Placebo |
|--|-----------------|------------------|
| | Started | 71 |
| Completed | 70 | 69 |
| Not completed | 1 | 2 |
| Consent withdrawn by subject | 1 | 2 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Phase I was a dose finding component and Phase II was an RCT. These were conducted separately on different populations and the numbers were not intended to be the same in this study.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Phase I Cohort 1 |
|-----------------------|------------------|

Reporting group description:

Saracatinib (AZD0530) 50mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days.

| | |
|-----------------------|------------------|
| Reporting group title | Phase I Cohort 2 |
|-----------------------|------------------|

Reporting group description:

Saracatinib (AZD0530) 125mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days

| | |
|-----------------------|------------------|
| Reporting group title | Phase I Cohort 3 |
|-----------------------|------------------|

Reporting group description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression),
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days

| | |
|-----------------------|-----------------|
| Reporting group title | Phase II Active |
|-----------------------|-----------------|

Reporting group description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|-----------------------|------------------|
| Reporting group title | Phase II Placebo |
|-----------------------|------------------|

Reporting group description:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
 Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
 Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
 Each cycle is 21 days after 7 day run-in period with placebo.

| Reporting group values | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 |
|---|------------------|------------------|------------------|
| Number of subjects | 3 | 3 | 4 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 1 | 1 |
| From 65-84 years | 3 | 2 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 3 | 3 | 4 |
| Phase II stratification factor: Presence of bone metastases | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | 0 | 0 | 0 |
| No | 0 | 0 | 0 |
| Not applicable | 3 | 3 | 4 |
| Phase II stratification factor: Presence of visceral (non-lymph node) disease | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | 0 | 0 | 0 |
| No | 0 | 0 | 0 |
| Not applicable | 3 | 3 | 4 |
| Baseline PSA | | | |
| Units: ng/mL | | | |
| median | 53.00 | 75.00 | 61.00 |
| inter-quartile range (Q1-Q3) | 9.00 to 90.00 | 15.00 to 179.60 | 53.00 to 273.70 |

| Reporting group values | Phase II Active | Phase II Placebo | Total |
|---|-----------------|------------------|-------|
| Number of subjects | 71 | 71 | 152 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 17 | 17 | 36 |
| From 65-84 years | 54 | 54 | 116 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 71 | 71 | 152 |
| Phase II stratification factor: Presence of bone metastases | | | |
| Only applicable to Phase II patients | | | |

| | | | |
|---|-----------------|-----------------|-----|
| Units: Subjects | | | |
| Yes | 64 | 63 | 127 |
| No | 7 | 8 | 15 |
| Not applicable | 0 | 0 | 10 |
| Phase II stratification factor: Presence of visceral (non-lymph node) disease | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | 15 | 16 | 31 |
| No | 56 | 55 | 111 |
| Not applicable | 0 | 0 | 10 |
| Baseline PSA | | | |
| Units: ng/mL | | | |
| median | 68.45 | 87.80 | |
| inter-quartile range (Q1-Q3) | 29.50 to 173.90 | 20.50 to 287.10 | - |

Subject analysis sets

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Phase I Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Phase I patients with one or more dose of study medication

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Phase I Evaluable Study Population |
| Subject analysis set type | Full analysis |

Subject analysis set description:

* Any patient who has experienced a DLT

* Any patient who has received two doses of docetaxel (with no more than 14 days delay in administration of the second dose)

* Any patient who has received at least 80% of scheduled doses of saracatinib within 42 days of first dose of docetaxel

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Phase II ITT Population |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Patients randomised on to the study

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Phase II Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Patients randomised on to the study with one or more dose of chemotherapy or study medication

| Reporting group values | Phase I Safety Population | Phase I Evaluable Study Population | Phase II ITT Population |
|--|---------------------------|------------------------------------|-------------------------|
| Number of subjects | 10 | 9 | 142 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 2 | 2 | 34 |

| | | | |
|-------------------|---|---|-----|
| From 65-84 years | 8 | 7 | 108 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|---|----|---|-----|
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 10 | 9 | 142 |
| Phase II stratification factor: Presence of bone metastases | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | | | |
| No | | | |
| Not applicable | | | |
| Phase II stratification factor: Presence of visceral (non-lymph node) disease | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | | | |
| No | | | |
| Not applicable | | | |
| Baseline PSA Units: ng/mL median inter-quartile range (Q1-Q3) | | | |

| | | | |
|---|----------------------------|--|--|
| Reporting group values | Phase II Safety Population | | |
| Number of subjects | 140 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 33 | | |
| From 65-84 years | 107 | | |
| 85 years and over | 0 | | |
| Gender categorical Units: Subjects | | | |
| Female | 0 | | |
| Male | 140 | | |
| Phase II stratification factor: Presence of bone metastases | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | | | |
| No | | | |
| Not applicable | | | |

| | | | |
|---|--|--|--|
| Phase II stratification factor: Presence of visceral (non-lymph node) disease | | | |
| Only applicable to Phase II patients | | | |
| Units: Subjects | | | |
| Yes | | | |
| No | | | |
| Not applicable | | | |
| Baseline PSA Units: ng/mL median inter-quartile range (Q1-Q3) | | | |

End points

End points reporting groups

| | |
|--|------------------|
| Reporting group title | Phase I Cohort 1 |
| Reporting group description: Saracatinib (AZD0530) 50mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days. | |
| Reporting group title | Phase I Cohort 2 |
| Reporting group description: Saracatinib (AZD0530) 125mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days | |
| Reporting group title | Phase I Cohort 3 |
| Reporting group description: Saracatinib (AZD0530) 175mg orally once daily continuously, starting on day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days | |
| Reporting group title | Phase II Active |
| Reporting group description: Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression, Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days after 7 day run-in period with Saracatinib. | |
| Reporting group title | Phase II Placebo |
| Reporting group description: Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression, Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days after 7 day run-in period with placebo. | |
| Reporting group title | Phase I Cohort 1 |
| Reporting group description: Saracatinib (AZD0530) 50mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression), Docetaxel 75mg/m ² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles), Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study. Each cycle is 21 days . | |
| Reporting group title | Phase I Cohort 2 |

Reporting group description:

Saracatinib (AZD0530) 125mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression),
Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
Each cycle is 21 days .

| | |
|-----------------------|------------------|
| Reporting group title | Phase I Cohort 3 |
|-----------------------|------------------|

Reporting group description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting on Day 11 of 1st cycle of docetaxel (continuing until disease progression),
Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
Each cycle is 21 days .

| | |
|-----------------------|-------------------|
| Reporting group title | Phase II Patients |
|-----------------------|-------------------|

Reporting group description:

Only required to overrule system error that requires the same number or fewer patients in a subsequent period: no summaries or analysis will be provided

| | |
|-----------------------|-----------------|
| Reporting group title | Phase II Active |
|-----------------------|-----------------|

Reporting group description:

Saracatinib (AZD0530) 175mg orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
Each cycle is 21 days after 7 day run-in period with Saracatinib.

| | |
|-----------------------|------------------|
| Reporting group title | Phase II Placebo |
|-----------------------|------------------|

Reporting group description:

Placebo orally once daily continuously, starting 7 days prior to 1st cycle of docetaxel i.e. Day -7 and continuing until disease progression,
Docetaxel 75mg/m² intravenously on Day 1 every 3 weeks (up to a maximum of 10 cycles),
Prednisolone 5mg orally twice daily continuously starting on Day 1 of 1st cycle of docetaxel (continuing for 21 days after last dose of docetaxel or beyond at Investigator's discretion). Both docetaxel and prednisolone are regarded as nIMPs within the study.
Each cycle is 21 days after 7 day run-in period with placebo.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Phase I Safety Population |
|----------------------------|---------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Phase I patients with one or more dose of study medication

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Phase I Evaluable Study Population |
|----------------------------|------------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

- * Any patient who has experienced a DLT
- * Any patient who has received two doses of docetaxel (with no more than 14 days delay in administration of the second dose)
- * Any patient who has received at least 80% of scheduled doses of saracatinib within 42 days of first dose of docetaxel

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Phase II ITT Population |
|----------------------------|-------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Patients randomised on to the study

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Phase II Safety Population |
|----------------------------|----------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Patients randomised on to the study with one or more dose of chemotherapy or study medication

Primary: Incidence of dose-limiting toxicities

| | |
|-----------------|---|
| End point title | Incidence of dose-limiting toxicities ^{[1][2]} |
|-----------------|---|

End point description:

Any of the following events occurring between the first administration of saracatinib and day 42 of first dose of study medication, if, in the opinion of the investigator, the event was due to the combination of saracatinib, docetaxel and prednisolone:

- * Greater than 14-day delay in administration of second dose of docetaxel due to drug toxicity
- * Grade 4 neutropenia \geq 7 days duration
- * Grade 3 – 4 neutropenia associated with an oral temperature \geq 38.5C
- * Grade 3 – 4 neutropenia associated with bacteriologically proven sepsis
- * Any grade 4 thrombocytopenia
- * Grade 3 thrombocytopenia associated with non-traumatic bleeding (except where this can be explained by therapeutic anticoagulation)
- * Any other clinically significant grade 3 or above toxicity except nausea or vomiting

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

End point timeframe:

Within 42 days of the first administration of saracatinib

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: Incidence of DLTs is reported using summary statistics only; no statistical analyses were performed on these data.

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

Justification: Incidence of DLTs is only relevant to the Phase I component of the study.

| End point values | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 | Phase I Evaluable Study Population |
|-----------------------------|------------------|------------------|------------------|------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 3 | 9 |
| Units: Patients | | | | |
| Patients | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Primary: Primary analysis: Progression-free survival

| | |
|-----------------|---|
| End point title | Primary analysis: Progression-free survival |
|-----------------|---|

End point description:

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

End point timeframe:

The primary endpoint is PFS, defined as the time from registration onto the study to progression (radiological progression or biochemical progression as defined by the PCWG21 criteria) or death from any cause, whichever occurs first.

| End point values | Phase II Active | Phase II Placebo | | |
|----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: Weeks | | | | |
| median (confidence interval 80%) | 19 (18 to 25) | 29 (20 to 32) | | |

Statistical analyses

| Statistical analysis title | Cox regression analysis |
|-----------------------------------|-------------------------|
|-----------------------------------|-------------------------|

Statistical analysis description:

A Cox regression model was fitted to the PFS data incorporating terms for study arm and the stratification factors used in the minimisation algorithm (presence of bone metastases, presence of visceral disease and site, which was reparameterised into sites reporting up to and including 10 patients versus those reporting more than 10 patients).

| | |
|---|------------------------------------|
| Comparison groups | Phase II Active v Phase II Placebo |
| Number of subjects included in analysis | 142 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.942 ^[3] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.323 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.053 |
| upper limit | 1.661 |

Notes:

[3] - One-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From consent until resolution, or for at least 30 days after discontinuation of study medication, whichever comes first or until toxicity has resolved to baseline or < Grade 1, or until the toxicity is considered to be irreversible.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

Reporting groups

| | |
|------------------------------|------------------|
| Reporting group title | Phase I Cohort 1 |
| Reporting group description: | - |
| Reporting group title | Phase I Cohort 2 |
| Reporting group description: | - |
| Reporting group title | Phase I Cohort 3 |
| Reporting group description: | - |
| Reporting group title | Phase II Active |
| Reporting group description: | - |
| Reporting group title | Phase II Placebo |
| Reporting group description: | - |

| Serious adverse events | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 |
|--|--|------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 2 / 4 (50.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | Additional description: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| HYPERTENSION | Additional description: HYPERTENSION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| THROMBOEMBOLIC EVENT | Additional description: THROMBOEMBOLIC EVENT | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOTENSION | Additional description: HYPOTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR DISORDERS - OTHER, SPECIFY | Additional description: VASCULAR DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| EDEMA LIMBS | Additional description: EDEMA LIMBS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| FATIGUE | Additional description: FATIGUE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEVER | Additional description: FEVER | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| FLU LIKE SYMPTOMS | Additional description: FLU LIKE SYMPTOMS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFUSION SITE EXTRAVASATION | Additional description: INFUSION SITE EXTRAVASATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MALAISE | Additional description: MALAISE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NON-CARDIAC CHEST PAIN | Additional description: NON-CARDIAC CHEST PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN | Additional description: PAIN | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| PELVIC PAIN | Additional description: PELVIC PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSPNEA | Additional description: DYSPNEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURAL EFFUSION | Additional description: PLEURAL EFFUSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPISTAXIS | Additional description: EPISTAXIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURITIC PAIN | Additional description: PLEURITIC PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PNEUMONITIS | Additional description: PNEUMONITIS | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PRODUCTIVE COUGH | Additional description: PRODUCTIVE COUGH | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | Additional description: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| DELIRIUM | Additional description: DELIRIUM | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INSOMNIA | Additional description: INSOMNIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | Additional description: ALANINE AMINOTRANSFERASE INCREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD BILIRUBIN INCREASED | Additional description: BLOOD BILIRUBIN INCREASED | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHOCYTE COUNT DECREASED | Additional description: LYMPHOCYTE COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLATELET COUNT DECREASED | Additional description: PLATELET COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPHIL COUNT DECREASED | Additional description: NEUTROPHIL COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| HIP FRACTURE | Additional description: HIP FRACTURE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | Additional description: ATRIAL FIBRILLATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| CHEST PAIN - CARDIAC | Additional description: CHEST PAIN - CARDIAC | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEART FAILURE | Additional description: HEART FAILURE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYOCARDIAL INFARCTION | Additional description: MYOCARDIAL INFARCTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PALPITATIONS | Additional description: PALPITATIONS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUS TACHYCARDIA | Additional description: SINUS TACHYCARDIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| ATAXIA | Additional description: ATAXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEPRESSED LEVEL OF CONSCIOUSNESS | Additional description: DEPRESSED LEVEL OF CONSCIOUSNESS | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| HEADACHE | Additional description: HEADACHE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | Additional description: NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LETHARGY | Additional description: LETHARGY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PARESTHESIA | Additional description: PARESTHESIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL MOTOR NEUROPATHY | Additional description: PERIPHERAL MOTOR NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL SENSORY NEUROPATHY | Additional description: PERIPHERAL SENSORY NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNCOPE | Additional description: SYNCOPE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| Blood and lymphatic system disorders | | | |
| ANEMIA | Additional description: ANEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEBRILE NEUTROPENIA | Additional description: FEBRILE NEUTROPENIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | Additional description: ABDOMINAL DISTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN | Additional description: ABDOMINAL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLONIC PERFORATION | Additional description: COLONIC PERFORATION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONSTIPATION | Additional description: CONSTIPATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHEA | Additional description: DIARRHEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC ULCER | Additional description: GASTRIC ULCER | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ILEAL OBSTRUCTION | Additional description: ILEAL OBSTRUCTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | Additional description: NAUSEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATITIS | Additional description: PANCREATITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--|---------------|---------------|
| RECTAL HEMORRHAGE | Additional description: RECTAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | Additional description: VOMITING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| SKIN ULCERATION | Additional description: SKIN ULCERATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | Additional description: ACUTE KIDNEY INJURY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEMATURIA | Additional description: HEMATURIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL AND URINARY DISORDERS - OTHER, SPECIFY | Additional description: RENAL AND URINARY DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY INCONTINENCE | Additional description: URINARY INCONTINENCE | | |

| | | | |
|--|---|----------------|---------------|
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | Additional description: ARTHRALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| AVASCULAR NECROSIS | Additional description: AVASCULAR NECROSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACK PAIN | Additional description: BACK PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHEST WALL PAIN | Additional description: CHEST WALL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | Additional description: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYALGIA | Additional description: MYALGIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| BRONCHIAL INFECTION | Additional description: BRONCHIAL INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | Additional description: INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| JOINT INFECTION | Additional description: JOINT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| LUNG INFECTION | Additional description: LUNG INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| SEPSIS | Additional description: SEPSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UPPER RESPIRATORY INFECTION | Additional description: UPPER RESPIRATORY INFECTION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN INFECTION | Additional description: SKIN INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | Additional description: URINARY TRACT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND INFECTION | Additional description: WOUND INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| ACIDOSIS | Additional description: ACIDOSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANOREXIA | Additional description: ANOREXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEHYDRATION | Additional description: DEHYDRATION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (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 |
| HYPERGLYCEMIA | Additional description: HYPERGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOCALCEMIA | Additional description: HYPOCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERKALEMIA | Additional description: HYPERKALEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOGLYCEMIA | Additional description: HYPOGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | Additional description: METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Phase II Active | Phase II Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 47 / 69 (68.12%) | 38 / 71 (53.52%) | |
| number of deaths (all causes) | 6 | 4 | |

| | | | |
|--|--|----------------|--|
| number of deaths resulting from adverse events | 3 | 3 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | Additional description: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Vascular disorders | | | |
| HYPERTENSION | Additional description: HYPERTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| THROMBOEMBOLIC EVENT | Additional description: THROMBOEMBOLIC EVENT | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 6 / 71 (8.45%) | |
| occurrences causally related to treatment / all | 2 / 4 | 4 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOTENSION | Additional description: HYPOTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VASCULAR DISORDERS - OTHER, SPECIFY | Additional description: VASCULAR DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| EDEMA LIMBS | Additional description: EDEMA LIMBS | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|-----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FATIGUE | Additional description: FATIGUE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEVER | Additional description: FEVER | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 8 / 71 (11.27%) | |
| occurrences causally related to treatment / all | 4 / 7 | 7 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FLU LIKE SYMPTOMS | Additional description: FLU LIKE SYMPTOMS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFUSION SITE EXTRAVASATION | Additional description: INFUSION SITE EXTRAVASATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MALAISE | Additional description: MALAISE | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|--|----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NON-CARDIAC CHEST PAIN | Additional description: NON-CARDIAC CHEST PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PAIN | Additional description: PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| PELVIC PAIN | Additional description: PELVIC PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSPNEA | Additional description: DYSPNEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 3 / 71 (4.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURAL EFFUSION | Additional description: PLEURAL EFFUSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EPISTAXIS | Additional description: EPISTAXIS | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURITIC PAIN | Additional description: PLEURITIC PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONITIS | Additional description: PNEUMONITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PRODUCTIVE COUGH | Additional description: PRODUCTIVE COUGH | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | Additional description: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| DELIRIUM | Additional description: DELIRIUM | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INSOMNIA | Additional description: INSOMNIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | Additional description: ALANINE AMINOTRANSFERASE INCREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BLOOD BILIRUBIN INCREASED | Additional description: BLOOD BILIRUBIN INCREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LYMPHOCYTE COUNT DECREASED | Additional description: LYMPHOCYTE COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLATELET COUNT DECREASED | Additional description: PLATELET COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NEUTROPHIL COUNT DECREASED | Additional description: NEUTROPHIL COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 16 / 69 (23.19%) | 7 / 71 (9.86%) | |
| occurrences causally related to treatment / all | 17 / 17 | 7 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| HIP FRACTURE | Additional description: HIP FRACTURE | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | Additional description: ATRIAL FIBRILLATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHEST PAIN - CARDIAC | Additional description: CHEST PAIN - CARDIAC | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEART FAILURE | Additional description: HEART FAILURE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYOCARDIAL INFARCTION | Additional description: MYOCARDIAL INFARCTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| PALPITATIONS | Additional description: PALPITATIONS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SINUS TACHYCARDIA | Additional description: SINUS TACHYCARDIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| ATAXIA | Additional description: ATAXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEPRESSED LEVEL OF CONSCIOUSNESS | Additional description: DEPRESSED LEVEL OF CONSCIOUSNESS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEADACHE | Additional description: HEADACHE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | Additional description: NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 3 / 71 (4.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LETHARGY | Additional description: LETHARGY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PARESTHESIA | Additional description: PARESTHESIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERIPHERAL MOTOR NEUROPATHY | Additional description: PERIPHERAL MOTOR NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERIPHERAL SENSORY NEUROPATHY | Additional description: PERIPHERAL SENSORY NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNCOPE | Additional description: SYNCOPE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 3 / 71 (4.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| ANEMIA | Additional description: ANEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEBRILE NEUTROPENIA | Additional description: FEBRILE NEUTROPENIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 7 / 71 (9.86%) | |
| occurrences causally related to treatment / all | 10 / 11 | 7 / 7 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | Additional description: ABDOMINAL DISTENSION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ABDOMINAL PAIN | Additional description: ABDOMINAL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COLONIC PERFORATION | Additional description: COLONIC PERFORATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| CONSTIPATION | Additional description: CONSTIPATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIARRHEA | Additional description: DIARRHEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 13 / 13 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRIC ULCER | Additional description: GASTRIC ULCER | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ILEAL OBSTRUCTION | Additional description: ILEAL OBSTRUCTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|----------------|--|
| NAUSEA | Additional description: NAUSEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PANCREATITIS | Additional description: PANCREATITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HEMORRHAGE | Additional description: RECTAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VOMITING | Additional description: VOMITING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 5 / 71 (7.04%) | |
| occurrences causally related to treatment / all | 5 / 6 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| SKIN ULCERATION | Additional description: SKIN ULCERATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | Additional description: ACUTE KIDNEY INJURY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 5 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| HEMATURIA | Additional description: HEMATURIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|--|----------------|--|
| subjects affected / exposed | 3 / 69 (4.35%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RENAL AND URINARY DISORDERS - OTHER, SPECIFY | Additional description: RENAL AND URINARY DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY INCONTINENCE | Additional description: URINARY INCONTINENCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | Additional description: ARTHRALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| AVASCULAR NECROSIS | Additional description: AVASCULAR NECROSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACK PAIN | Additional description: BACK PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 3 / 71 (4.23%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHEST WALL PAIN | Additional description: CHEST WALL PAIN | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | Additional description: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYALGIA | Additional description: MYALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| BRONCHIAL INFECTION | Additional description: BRONCHIAL INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | Additional description: INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 2 / 5 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| JOINT INFECTION | Additional description: JOINT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUNG INFECTION | Additional description: LUNG INFECTION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 8 / 69 (11.59%) | 4 / 71 (5.63%) | |
| occurrences causally related to treatment / all | 7 / 8 | 2 / 6 | |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | |
| SEPSIS | Additional description: SEPSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 5 / 71 (7.04%) | |
| occurrences causally related to treatment / all | 4 / 4 | 5 / 5 | |
| deaths causally related to treatment / all | 1 / 1 | 2 / 2 | |
| UPPER RESPIRATORY INFECTION | Additional description: UPPER RESPIRATORY INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SKIN INFECTION | Additional description: SKIN INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION | Additional description: URINARY TRACT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WOUND INFECTION | Additional description: WOUND INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| ACIDOSIS | Additional description: ACIDOSIS | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---------------------------------------|----------------|--|
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANOREXIA | Additional description: ANOREXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEHYDRATION | Additional description: DEHYDRATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERGLYCEMIA | Additional description: HYPERGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| HYPOCALCEMIA | Additional description: HYPOCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERKALEMIA | Additional description: HYPERKALEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOGLYCEMIA | Additional description: HYPOGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|----------------|--|
| METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | Additional description: METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Phase I Cohort 1 | Phase I Cohort 2 | Phase I Cohort 3 |
|--|--|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 3 / 3 (100.00%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | Additional description: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| HOT FLASHES | Additional description: HOT FLASHES | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERTENSION | Additional description: HYPERTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOTENSION | Additional description: HYPOTENSION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PHLEBITIS | Additional description: PHLEBITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |

| | | | |
|--|---|---------------------|-----------------------|
| LYMPHEDEMA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: LYMPHEDEMA | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| THROMBOEMBOLIC EVENT alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: THROMBOEMBOLIC EVENT | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| EDEMA FACE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EDEMA FACE | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| CHILLS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: CHILLS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| EDEMA LIMBS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EDEMA LIMBS | | |
| | 1 / 3 (33.33%) 2 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| FATIGUE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: FATIGUE | | |
| | 3 / 3 (100.00%) 12 | 2 / 3 (66.67%) 6 | 4 / 4 (100.00%) 17 |
| FEVER alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: FEVER | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | | |
| | 2 / 3 (66.67%) 2 | 1 / 3 (33.33%) 1 | 3 / 4 (75.00%) 6 |
| FLU LIKE SYMPTOMS | Additional description: FLU LIKE SYMPTOMS | | |

| | | | |
|---|--|--------------------|---------------------|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| MALAISE | Additional description: MALAISE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| NON-CARDIAC CHEST PAIN | Additional description: NON-CARDIAC CHEST PAIN | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PAIN | Additional description: PAIN | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 2 |
| Immune system disorders | | | |
| ALLERGIC REACTION | Additional description: ALLERGIC REACTION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| PELVIC PAIN | Additional description: PELVIC PAIN | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | Additional description: COUGH | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 3 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DYSPNEA | Additional description: DYSPNEA | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| | | | |
|---|--|--------------------|--------------------|
| EPISTAXIS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EPISTAXIS | | |
| | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PNEUMONITIS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: PNEUMONITIS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| SINUS DISORDER alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: SINUS DISORDER | | |
| | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| SORE THROAT alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: SORE THROAT | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Psychiatric disorders | | | |
| ANXIETY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: ANXIETY | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| INSOMNIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: INSOMNIA | | |
| | 1 / 3 (33.33%) 2 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DEPRESSION alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: DEPRESSION | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PSYCHIATRIC DISORDERS - OTHER, SPECIFY | Additional description: PSYCHIATRIC DISORDERS - OTHER, SPECIFY | | |

| | | | |
|---|--|--------------------|---------------------|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PERSONALITY CHANGE | Additional description: PERSONALITY CHANGE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | Additional description: ALANINE AMINOTRANSFERASE INCREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| ALKALINE PHOSPHATASE INCREASED | Additional description: ALKALINE PHOSPHATASE INCREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| ASPARTATE AMINOTRANSFERASE INCREASED | Additional description: ASPARTATE AMINOTRANSFERASE INCREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| WEIGHT GAIN | Additional description: WEIGHT GAIN | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| NEUTROPHIL COUNT DECREASED | Additional description: NEUTROPHIL COUNT DECREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| WHITE BLOOD CELL DECREASED | Additional description: WHITE BLOOD CELL DECREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| WEIGHT LOSS | Additional description: WEIGHT LOSS | | |

| | | | |
|---|--|---------------------|--------------------|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| BRUISING | Additional description: BRUISING | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| FALL | Additional description: FALL | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cardiac disorders | | | |
| CARDIAC DISORDERS - OTHER, SPECIFY | Additional description: CARDIAC DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| CHEST PAIN - CARDIAC | Additional description: CHEST PAIN - CARDIAC | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nervous system disorders | | | |
| COGNITIVE DISTURBANCE | Additional description: COGNITIVE DISTURBANCE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| CONCENTRATION IMPAIRMENT | Additional description: CONCENTRATION IMPAIRMENT | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DIZZINESS | Additional description: DIZZINESS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |

| | | | |
|--|---|---------------------|---------------------|
| HEADACHE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: HEADACHE | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DYSGEUSIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: DYSGEUSIA | | |
| | 1 / 3 (33.33%) 3 | 1 / 3 (33.33%) 2 | 1 / 4 (25.00%) 1 |
| LETHARGY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: LETHARGY | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 2 / 4 (50.00%) 2 |
| MEMORY IMPAIRMENT alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: MEMORY IMPAIRMENT | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | | |
| | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PARESTHESIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: PARESTHESIA | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PERIPHERAL MOTOR NEUROPATHY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: PERIPHERAL MOTOR NEUROPATHY | | |
| | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| PERIPHERAL SENSORY NEUROPATHY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: PERIPHERAL SENSORY NEUROPATHY | | |
| | 2 / 3 (66.67%) 7 | 1 / 3 (33.33%) 2 | 1 / 4 (25.00%) 3 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---|---------------------|--------------------|
| ANEMIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: ANEMIA | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: BLOOD AND LYMPHATIC SYSTEM DISORDERS - OTHER, SPECIFY | | |
| | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |
| FEBRILE NEUTROPENIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: FEBRILE NEUTROPENIA | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| LEUKOCYTOSIS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: LEUKOCYTOSIS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| THROMBOTIC THROMBOCYTOPENIC PURPURA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: THROMBOTIC THROMBOCYTOPENIC PURPURA | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Ear and labyrinth disorders HEARING IMPAIRED alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: HEARING IMPAIRED | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| | Additional description: TINNITUS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| VESTIBULAR DISORDER alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: VESTIBULAR DISORDER | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Eye disorders | | | |

| | | | |
|---|--|--------------------|---------------------|
| BLURRED VISION alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: BLURRED VISION | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| CONJUNCTIVITIS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: CONJUNCTIVITIS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DRY EYE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: DRY EYE | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| EXTRAOCULAR MUSCLE PARESIS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EXTRAOCULAR MUSCLE PARESIS | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| EYE DISORDERS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EYE DISORDERS - OTHER, SPECIFY | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| EYE PAIN alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: EYE PAIN | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| WATERING EYES alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: WATERING EYES | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastrointestinal disorders ABDOMINAL PAIN alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: ABDOMINAL PAIN | | |
| | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| BLOATING alternative assessment type: Non-systematic | Additional description: BLOATING | | |
| | | | |

| | | | |
|---|--|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CHEILITIS | Additional description: CHEILITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | Additional description: CONSTIPATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 0 | 2 |
| DIARRHEA | Additional description: DIARRHEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 4 / 4 (100.00%) |
| occurrences (all) | 1 | 1 | 12 |
| DYSPEPSIA | Additional description: DYSPEPSIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| DRY MOUTH | Additional description: DRY MOUTH | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| FLATULENCE | Additional description: FLATULENCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FECAL INCONTINENCE | Additional description: FECAL INCONTINENCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTRITIS | Additional description: GASTRITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---|----------------|----------------|
| GASTROESOPHAGEAL REFLUX DISEASE | Additional description: GASTROESOPHAGEAL REFLUX DISEASE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| GASTROINTESTINAL DISORDERS - OTHER, SPECIFY | Additional description: GASTROINTESTINAL DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| MUCOSITIS ORAL | Additional description: MUCOSITIS ORAL | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 7 | 0 | 1 |
| NAUSEA | Additional description: NAUSEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 2 | 7 |
| ORAL PAIN | Additional description: ORAL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL HEMORRHAGE | Additional description: ORAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SALIVARY DUCT INFLAMMATION | Additional description: SALIVARY DUCT INFLAMMATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RECTAL HEMORRHAGE | Additional description: RECTAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | Additional description: VOMITING | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| STOMACH PAIN | Additional description: STOMACH PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| HEPATOBIILIARY DISORDERS - OTHER, SPECIFY | Additional description: HEPATOBIILIARY DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | Additional description: ALOPECIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 1 / 3 (33.33%) | 3 / 4 (75.00%) |
| occurrences (all) | 9 | 5 | 15 |
| DRY SKIN | Additional description: DRY SKIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 0 | 3 |
| ERYTHEMA MULTIFORME | Additional description: ERYTHEMA MULTIFORME | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL DISCOLORATION | Additional description: NAIL DISCOLORATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NAIL LOSS | Additional description: NAIL LOSS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL RIDGING | Additional description: NAIL RIDGING | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRURITUS | Additional description: PRURITUS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME | Additional description: PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH MACULO-PAPULAR | Additional description: RASH MACULO-PAPULAR | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| RASH ACNEIFORM | Additional description: RASH ACNEIFORM | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS - OTHER, SPECIFY | Additional description: SKIN AND SUBCUTANEOUS TISSUE DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Renal and urinary disorders | | | |
| URINARY FREQUENCY | Additional description: URINARY FREQUENCY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEMATURIA | Additional description: HEMATURIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE DISCOLORATION | Additional description: URINE DISCOLORATION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Endocrine disorders | | | |
| CUSHINGOID | Additional description: CUSHINGOID | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | Additional description: ARTHRALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| BONE PAIN | Additional description: BONE PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | Additional description: BACK PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| GENERALIZED MUSCLE WEAKNESS | Additional description: GENERALIZED MUSCLE WEAKNESS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CHEST WALL PAIN | Additional description: CHEST WALL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE WEAKNESS LOWER LIMB | Additional description: MUSCLE WEAKNESS LOWER LIMB | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE WEAKNESS UPPER LIMB | Additional description: MUSCLE WEAKNESS UPPER LIMB | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | Additional description: MYALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | Additional description: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN IN EXTREMITY | Additional description: PAIN IN EXTREMITY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Infections and infestations | | | |
| INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | Additional description: INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 2 | 0 | 3 |
| MUCOSAL INFECTION | Additional description: MUCOSAL INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL INFECTION | Additional description: NAIL INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PARONYCHIA | Additional description: PARONYCHIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN INFECTION | Additional description: SKIN INFECTION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINITIS INFECTIVE | Additional description: RHINITIS INFECTIVE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TOOTH INFECTION | Additional description: TOOTH INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY INFECTION | Additional description: UPPER RESPIRATORY INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT INFECTION | Additional description: URINARY TRACT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| ANOREXIA | Additional description: ANOREXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 3 | 1 | 3 |
| GLUCOSE INTOLERANCE | Additional description: GLUCOSE INTOLERANCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERCALCEMIA | Additional description: HYPERCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERGLYCEMIA | Additional description: HYPERGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOCALCEMIA | Additional description: HYPOCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOPHOSPHATEMIA | Additional description: HYPOPHOSPHATEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOKALEMIA | Additional description: HYPOKALEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | Additional description: METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Phase II Active | Phase II Placebo | |
|---|--|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 61 / 69 (88.41%) | 68 / 71 (95.77%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | Additional description: NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| HOT FLASHES | Additional description: HOT FLASHES | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 3 / 69 (4.35%) | 2 / 71 (2.82%) | |
| occurrences (all) | 8 | 3 | |
| ----- | | | |
| HYPERTENSION | | | |
| Additional description: HYPERTENSION | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 4 / 71 (5.63%) | |
| occurrences (all) | 10 | 16 | |
| ----- | | | |
| HYPOTENSION | | | |
| Additional description: HYPOTENSION | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| ----- | | | |
| PHLEBITIS | | | |
| Additional description: PHLEBITIS | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| ----- | | | |
| LYMPHEDEMA | | | |
| Additional description: LYMPHEDEMA | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| ----- | | | |
| THROMBOEMBOLIC EVENT | | | |
| Additional description: THROMBOEMBOLIC EVENT | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 1 / 71 (1.41%) | |
| occurrences (all) | 3 | 1 | |
| ----- | | | |
| General disorders and administration site conditions | | | |
| EDEMA FACE | | | |
| Additional description: EDEMA FACE | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| ----- | | | |
| CHILLS | | | |
| Additional description: CHILLS | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| ----- | | | |
| EDEMA LIMBS | | | |
| Additional description: EDEMA LIMBS | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|------------------|--|
| subjects affected / exposed | 3 / 69 (4.35%) | 2 / 71 (2.82%) | |
| occurrences (all) | 8 | 4 | |
| FATIGUE | Additional description: FATIGUE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 49 / 69 (71.01%) | 54 / 71 (76.06%) | |
| occurrences (all) | 238 | 292 | |
| FEVER | Additional description: FEVER | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 4 / 71 (5.63%) | |
| occurrences (all) | 7 | 4 | |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 28 / 69 (40.58%) | 26 / 71 (36.62%) | |
| occurrences (all) | 77 | 65 | |
| FLU LIKE SYMPTOMS | Additional description: FLU LIKE SYMPTOMS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| MALAISE | Additional description: MALAISE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| NON-CARDIAC CHEST PAIN | Additional description: NON-CARDIAC CHEST PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences (all) | 2 | 1 | |
| PAIN | Additional description: PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 8 / 71 (11.27%) | |
| occurrences (all) | 17 | 15 | |
| Immune system disorders | | | |
| ALLERGIC REACTION | Additional description: ALLERGIC REACTION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 2 | 0 / 71 (0.00%) 0 | |
| Reproductive system and breast disorders | | | |
| PELVIC PAIN | Additional description: PELVIC PAIN | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 71 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | Additional description: COUGH | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 10 / 69 (14.49%) 23 | 4 / 71 (5.63%) 12 | |
| DYSPNEA | Additional description: DYSPNEA | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 11 / 69 (15.94%) 28 | 6 / 71 (8.45%) 13 | |
| EPISTAXIS | Additional description: EPISTAXIS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 6 / 69 (8.70%) 14 | 3 / 71 (4.23%) 9 | |
| PNEUMONITIS | Additional description: PNEUMONITIS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 4 | 0 / 71 (0.00%) 0 | |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | Additional description: RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 8 / 69 (11.59%) 24 | 7 / 71 (9.86%) 17 | |
| SINUS DISORDER | Additional description: SINUS DISORDER | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 71 (0.00%) 0 | |
| SORE THROAT | Additional description: SORE THROAT | | |

| | | | |
|---|--|----------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 5 | 3 / 71 (4.23%) 5 | |
| Psychiatric disorders | | | |
| ANXIETY | Additional description: ANXIETY | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| INSOMNIA | Additional description: INSOMNIA | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 9 / 69 (13.04%) 25 | 3 / 71 (4.23%) 16 | |
| DEPRESSION | Additional description: DEPRESSION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 1 / 71 (1.41%) 1 | |
| PSYCHIATRIC DISORDERS - OTHER, SPECIFY | Additional description: PSYCHIATRIC DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 4 | |
| PERSONALITY CHANGE | Additional description: PERSONALITY CHANGE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | Additional description: ALANINE AMINOTRANSFERASE INCREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 3 | 1 / 71 (1.41%) 1 | |
| ALKALINE PHOSPHATASE INCREASED | Additional description: ALKALINE PHOSPHATASE INCREASED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| ASPARTATE AMINOTRANSFERASE | Additional description: ASPARTATE AMINOTRANSFERASE INCREASED | | |

| | | | |
|--|--|----------------|--|
| INCREASED | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| WEIGHT GAIN | Additional description: WEIGHT GAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 2 | |
| NEUTROPHIL COUNT DECREASED | Additional description: NEUTROPHIL COUNT DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 2 / 71 (2.82%) | |
| occurrences (all) | 8 | 2 | |
| WHITE BLOOD CELL DECREASED | Additional description: WHITE BLOOD CELL DECREASED | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| WEIGHT LOSS | Additional description: WEIGHT LOSS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 2 / 71 (2.82%) | |
| occurrences (all) | 3 | 2 | |
| Injury, poisoning and procedural complications | | | |
| BRUISING | Additional description: BRUISING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 6 / 71 (8.45%) | |
| occurrences (all) | 22 | 17 | |
| FALL | Additional description: FALL | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |
| CARDIAC DISORDERS - OTHER, SPECIFY | Additional description: CARDIAC DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |

| | | |
|--|---|------------------------|
| CHEST PAIN - CARDIAC alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: CHEST PAIN - CARDIAC | |
| | 2 / 69 (2.90%) 2 | 0 / 71 (0.00%) 0 |
| Nervous system disorders COGNITIVE DISTURBANCE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: COGNITIVE DISTURBANCE | |
| | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 |
| CONCENTRATION IMPAIRMENT alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: CONCENTRATION IMPAIRMENT | |
| | 1 / 69 (1.45%) 2 | 1 / 71 (1.41%) 1 |
| DIZZINESS alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: DIZZINESS | |
| | 5 / 69 (7.25%) 11 | 5 / 71 (7.04%) 10 |
| HEADACHE alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: HEADACHE | |
| | 5 / 69 (7.25%) 6 | 4 / 71 (5.63%) 7 |
| DYSGEUSIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: DYSGEUSIA | |
| | 27 / 69 (39.13%) 94 | 23 / 71 (32.39%) 78 |
| LETHARGY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: LETHARGY | |
| | 4 / 69 (5.80%) 4 | 2 / 71 (2.82%) 2 |
| MEMORY IMPAIRMENT alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: MEMORY IMPAIRMENT | |
| | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 3 |
| NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY alternative assessment type: Non- | Additional description: NERVOUS SYSTEM DISORDERS - OTHER, SPECIFY | |
| | | |

| | | | |
|--|---|------------------|--|
| systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 71 (1.41%) | |
| occurrences (all) | 1 | 1 | |
| PARESTHESIA | Additional description: PARESTHESIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 3 / 71 (4.23%) | |
| occurrences (all) | 2 | 4 | |
| PERIPHERAL MOTOR NEUROPATHY | Additional description: PERIPHERAL MOTOR NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 10 / 71 (14.08%) | |
| occurrences (all) | 9 | 13 | |
| PERIPHERAL SENSORY NEUROPATHY | Additional description: PERIPHERAL SENSORY NEUROPATHY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 23 / 69 (33.33%) | 29 / 71 (40.85%) | |
| occurrences (all) | 80 | 147 | |
| Blood and lymphatic system disorders | | | |
| ANEMIA | Additional description: ANEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 4 / 71 (5.63%) | |
| occurrences (all) | 14 | 16 | |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS - OTHER, SPECIFY | Additional description: BLOOD AND LYMPHATIC SYSTEM DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 3 / 71 (4.23%) | |
| occurrences (all) | 2 | 12 | |
| FEBRILE NEUTROPENIA | Additional description: FEBRILE NEUTROPENIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| LEUKOCYTOSIS | Additional description: LEUKOCYTOSIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| THROMBOTIC THROMBOCYTOPENIC PURPURA | Additional description: THROMBOTIC THROMBOCYTOPENIC PURPURA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| Ear and labyrinth disorders | | | |
| HEARING IMPAIRED | Additional description: HEARING IMPAIRED | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| TINNITUS | Additional description: TINNITUS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| VESTIBULAR DISORDER | Additional description: VESTIBULAR DISORDER | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 | |
| Eye disorders | | | |
| BLURRED VISION | Additional description: BLURRED VISION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 5 | 1 / 71 (1.41%) 2 | |
| CONJUNCTIVITIS | Additional description: CONJUNCTIVITIS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 2 / 71 (2.82%) 2 | |
| DRY EYE | Additional description: DRY EYE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 2 | 3 / 71 (4.23%) 10 | |
| EXTRAOCULAR MUSCLE PARESIS | Additional description: EXTRAOCULAR MUSCLE PARESIS | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 | |
| EYE DISORDERS - OTHER, SPECIFY | Additional description: EYE DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|------------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 71 (2.82%) | |
| occurrences (all) | 0 | 4 | |
| EYE PAIN | Additional description: EYE PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| WATERING EYES | Additional description: WATERING EYES | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 5 / 71 (7.04%) | |
| occurrences (all) | 9 | 23 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | Additional description: ABDOMINAL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences (all) | 3 | 1 | |
| BLOATING | Additional description: BLOATING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 5 | |
| CHEILITIS | Additional description: CHEILITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 3 | |
| CONSTIPATION | Additional description: CONSTIPATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | 5 / 71 (7.04%) | |
| occurrences (all) | 27 | 11 | |
| DIARRHEA | Additional description: DIARRHEA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 35 / 69 (50.72%) | 36 / 71 (50.70%) | |
| occurrences (all) | 104 | 87 | |
| DYSPEPSIA | Additional description: DYSPEPSIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|------------------|--|
| subjects affected / exposed | 6 / 69 (8.70%) | 11 / 71 (15.49%) | |
| occurrences (all) | 10 | 29 | |
| DRY MOUTH | Additional description: DRY MOUTH | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 2 / 71 (2.82%) | |
| occurrences (all) | 21 | 9 | |
| FLATULENCE | Additional description: FLATULENCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 71 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| FECAL INCONTINENCE | Additional description: FECAL INCONTINENCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| GASTRITIS | Additional description: GASTRITIS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| GASTROESOPHAGEAL REFLUX DISEASE | Additional description: GASTROESOPHAGEAL REFLUX DISEASE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| GASTROINTESTINAL DISORDERS - OTHER, SPECIFY | Additional description: GASTROINTESTINAL DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 4 / 71 (5.63%) | |
| occurrences (all) | 4 | 13 | |
| MUCOSITIS ORAL | Additional description: MUCOSITIS ORAL | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 11 / 71 (15.49%) | |
| occurrences (all) | 22 | 25 | |
| NAUSEA | Additional description: NAUSEA | | |
| alternative assessment type: Non-systematic | | | |

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|---|--|------------------|--|
| subjects affected / exposed | 23 / 69 (33.33%) | 26 / 71 (36.62%) | |
| occurrences (all) | 47 | 71 | |
| ORAL PAIN | Additional description: ORAL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 7 / 71 (9.86%) | |
| occurrences (all) | 3 | 21 | |
| ORAL HEMORRHAGE | Additional description: ORAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| SALIVARY DUCT INFLAMMATION | Additional description: SALIVARY DUCT INFLAMMATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 71 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| RECTAL HEMORRHAGE | Additional description: RECTAL HEMORRHAGE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 2 / 71 (2.82%) | |
| occurrences (all) | 8 | 2 | |
| VOMITING | Additional description: VOMITING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 13 / 71 (18.31%) | |
| occurrences (all) | 15 | 16 | |
| STOMACH PAIN | Additional description: STOMACH PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hepatobiliary disorders | Additional description: HEPATOBILIARY DISORDERS - OTHER, SPECIFY | | |
| HEPATOBILIARY DISORDERS - OTHER, SPECIFY | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Skin and subcutaneous tissue disorders | Additional description: ALOPECIA | | |
| ALOPECIA | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|------------------|--|
| subjects affected / exposed | 24 / 69 (34.78%) | 31 / 71 (43.66%) | |
| occurrences (all) | 118 | 155 | |
| DRY SKIN | Additional description: DRY SKIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 3 / 71 (4.23%) | |
| occurrences (all) | 3 | 19 | |
| ERYTHEMA MULTIFORME | Additional description: ERYTHEMA MULTIFORME | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 2 / 71 (2.82%) | |
| occurrences (all) | 0 | 2 | |
| NAIL DISCOLORATION | Additional description: NAIL DISCOLORATION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 6 / 71 (8.45%) | |
| occurrences (all) | 18 | 24 | |
| NAIL LOSS | Additional description: NAIL LOSS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences (all) | 1 | 3 | |
| NAIL RIDGING | Additional description: NAIL RIDGING | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 9 / 71 (12.68%) | |
| occurrences (all) | 5 | 43 | |
| PRURITUS | Additional description: PRURITUS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME | Additional description: PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 0 / 71 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| RASH MACULO-PAPULAR | Additional description: RASH MACULO-PAPULAR | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 6 / 71 (8.45%) | |
| occurrences (all) | 14 | 8 | |

| | | |
|---|---|---------------------|
| RASH ACNEIFORM alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: RASH ACNEIFORM | |
| | 0 / 69 (0.00%) 0 | 2 / 71 (2.82%) 4 |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS - OTHER, SPECIFY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: SKIN AND SUBCUTANEOUS TISSUE DISORDERS - OTHER, SPECIFY | |
| | 4 / 69 (5.80%) 7 | 6 / 71 (8.45%) 7 |
| Renal and urinary disorders | | |
| URINARY FREQUENCY alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: URINARY FREQUENCY | |
| | 1 / 69 (1.45%) 1 | 1 / 71 (1.41%) 1 |
| HEMATURIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: HEMATURIA | |
| | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 |
| URINE DISCOLORATION alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: URINE DISCOLORATION | |
| | 1 / 69 (1.45%) 3 | 0 / 71 (0.00%) 0 |
| Endocrine disorders | | |
| CUSHINGOID alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: CUSHINGOID | |
| | 1 / 69 (1.45%) 1 | 1 / 71 (1.41%) 1 |
| Musculoskeletal and connective tissue disorders | | |
| ARTHRALGIA alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: ARTHRALGIA | |
| | 1 / 69 (1.45%) 1 | 1 / 71 (1.41%) 1 |
| BONE PAIN alternative assessment type: Non-systematic | Additional description: BONE PAIN | |
| | | |

| | | | |
|--|---|------------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| BACK PAIN | Additional description: BACK PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences (all) | 1 | 3 | |
| GENERALIZED MUSCLE WEAKNESS | Additional description: GENERALIZED MUSCLE WEAKNESS | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 1 / 71 (1.41%) | |
| occurrences (all) | 3 | 1 | |
| CHEST WALL PAIN | Additional description: CHEST WALL PAIN | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 2 / 71 (2.82%) | |
| occurrences (all) | 2 | 2 | |
| MUSCLE WEAKNESS LOWER LIMB | Additional description: MUSCLE WEAKNESS LOWER LIMB | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 71 (1.41%) | |
| occurrences (all) | 4 | 2 | |
| MUSCLE WEAKNESS UPPER LIMB | Additional description: MUSCLE WEAKNESS UPPER LIMB | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| MYALGIA | Additional description: MYALGIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 10 / 71 (14.08%) | |
| occurrences (all) | 12 | 27 | |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | Additional description: MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 4 / 71 (5.63%) | |
| occurrences (all) | 2 | 12 | |
| PAIN IN EXTREMITY | Additional description: PAIN IN EXTREMITY | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|--|-----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 2 | 0 / 71 (0.00%) 0 | |
| Infections and infestations | | | |
| INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | Additional description: INFECTIONS AND INFESTATIONS - OTHER, SPECIFY | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 8 / 69 (11.59%) 9 | 8 / 71 (11.27%) 10 | |
| MUCOSAL INFECTION | Additional description: MUCOSAL INFECTION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| NAIL INFECTION | Additional description: NAIL INFECTION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 6 / 71 (8.45%) 7 | |
| PARONYCHIA | Additional description: PARONYCHIA | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 2 / 71 (2.82%) 2 | |
| SKIN INFECTION | Additional description: SKIN INFECTION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| RHINITIS INFECTIVE | Additional description: RHINITIS INFECTIVE | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 1 / 71 (1.41%) 1 | |
| TOOTH INFECTION | Additional description: TOOTH INFECTION | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 | |
| UPPER RESPIRATORY INFECTION | Additional description: UPPER RESPIRATORY INFECTION | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|------------------|--|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| URINARY TRACT INFECTION | Additional description: URINARY TRACT INFECTION | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 71 (1.41%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| ANOREXIA | Additional description: ANOREXIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 20 / 69 (28.99%) | 17 / 71 (23.94%) | |
| occurrences (all) | 35 | 43 | |
| GLUCOSE INTOLERANCE | Additional description: GLUCOSE INTOLERANCE | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 71 (1.41%) | |
| occurrences (all) | 1 | 2 | |
| HYPERCALCEMIA | Additional description: HYPERCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| HYPERGLYCEMIA | Additional description: HYPERGLYCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 71 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| HYPOCALCEMIA | Additional description: HYPOCALCEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 71 (1.41%) | |
| occurrences (all) | 1 | 1 | |
| HYPOPHOSPHATEMIA | Additional description: HYPOPHOSPHATEMIA | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 69 (4.35%) | 0 / 71 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| HYPOKALEMIA | Additional description: HYPOKALEMIA | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|--|-----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 69 (1.45%) 1 | 0 / 71 (0.00%) 0 | |
| METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | Additional description: METABOLISM AND NUTRITION DISORDERS - OTHER, SPECIFY | | |
| alternative assessment type: Non- systematic | | | |
| subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 71 (1.41%) 1 | |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed occurrences (all) | 2 / 69 (2.90%) 5 | 8 / 71 (11.27%) 36 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 19 August 2014 | As per the original study protocol, patients that are un-blinded should discontinue study treatment - this has been clarified in the amended protocol. Update on the information provided for emergency un-blinding of patients to highlight that sites will need log in details for the IVRS system. Information added on wash out periods for Abiraterone and Bicalutamide. Dose Reduction section made clearer at request of sites Updated PV section for clarity and to give further guidance on pregnancy of patients partners. |
| 28 July 2017 | Visit schedule during maintenance therapy updated to allow 6-weekly visits. Clarification of AE reporting requirements during follow-up. PV section updated in line with current CRUK CTU Glasgow template. Recruitment period changed to 30 months from 18 months to reflect actual time. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported