# Clinical trial results:
# A Single Arm, Open-Label, Phase 2 Study of Melflufen in Combination with Dexamethasone in Patients with Relapsed Refractory Multiple Myeloma who are Refractory to Pomalidomide and/or an anti-CD38 Monoclonal Antibody

## Summary

| | |
|---|---|
| EudraCT number | 2016-000965-21 |
| Trial protocol | ES FR IT |
| Global end of trial date | 16 November 2021 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 11 September 2022 |
| First version publication date | 11 September 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | OP-106 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02963493 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Oncopeptides AB |
| Sponsor organisation address | Västra Trädgårdsgatan 15, Stockholm, Sweden, |
| Public contact | Chief Operating Officer, Oncopeptides AB, trials@oncopeptides.com |
| Scientific contact | Chief Operating Officer, Oncopeptides AB, trials@oncopeptides.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 02 February 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 November 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this single-arm, Phase 2 study was to evaluate the efficacy (overall response rate [ORR]) of melflufen treatment in relapsed-refractory multiple myeloma (RRMM) patients. ORR was defined as the proportion of patients for whom the best overall confirmed response to treatment with melflufen was stringent complete response (sCR), complete response (CR), very good partial response (VGPR) or partial response (PR).

Protection of trial subjects:

Prior to the initiation of any trial-specific procedures, all participating trial subject were required to sign an informed consent that had previously been reviewed and approved by an ethics committee.
The safety, dose and dosing schedule of melflufen and dexamethasone in RRMM had previously been evaluated in a clinical study with patients having late-stage relapsed and relapsed refractory multiple myeloma (RRMM). The current study was designed based on well-established guidance for oncology studies including RRMM management, response assessment, and National Comprehensive Cancer Network Guidelines. Safety was monitored through the following safety assessments: documentation and follow-up of AEs and SAEs, physical examination (vital sign measurements and assessment of ECOG PS and neurological status), chest radiographs, 12-lead ECG, routine safety laboratory tests including additional reporting requirements of Grade 3 and 4 thrombocytopenia and neutropenia.
Any AE that occurred after the first dose of study medication up to 30 days after the last study drug administration was recorded in the CRF and was followed for 30 days after the last study drug administration or until resolution, whichever came first.
Laboratory abnormalities assessed as clinically significant were also recorded as adverse events. The Investigator recorded the grade of each clinically significant laboratory abnormality and evaluated any relationship to the study drug and clinical condition.
Results were published only at a group level with no availability of individual patient data.

Background therapy:

Patients with Relapsed Refractory Multiple Myeloma (RRMM) often have disease that is refractory to multiple drugs. In earlier treatment lines, novel agents are commonly administered in combination, resulting in disease resistant to multiple drug classes.
Therefore, there is an urgent need to develop new therapies with different safety and tolerability profiles for patients with late-stage RRMM who have exhausted available therapies.
Melflufen combined with dexamethasone, has the potential to fill this unmet medical need by providing a novel mechanism of action, clinically meaningful efficacy, and manageable safety in patients with RRMM.

Evidence for comparator:

No comparator was used in the current study.

| | |
|---|---|
| Actual start date of recruitment | 28 December 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 52 |
| Country: Number of subjects enrolled | France: 13 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | United States: 69 |
| Worldwide total number of subjects | 157 |
| EEA total number of subjects | 88 |

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) | 78 |
| From 65 to 84 years | 78 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted by 16 Investigators at 17 sites (one Investigator enrolled patients at 2 sites) and patients were enrolled in France, Italy, Spain, and the United States.
The first patient initiated study treatment on December 28, 2016 and the date for last patient last visit was November 16, 2021.

### Pre-assignment

Screening details:

Screening assessments were performed between Day -21 and Day -1. The purpose of the Screening Period was to obtain informed consent and to establish protocol eligibility. Out of the 215 screened subjects, 165 met the eligibility criteria and 157 were enrolled in the study.

### Period 1

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

Blinding implementation details:

This was a single-arm, open-label study and therefore no blinding was implemented.

### Arms

| | |
|---|---|
| **Arm title** | Treatment |

Arm description:

This was a single-arm study and all enrolled subjects/patients were treated with 28-day cycles of therapy with melflufen on Day 1 and dexamethasone on Days 1, 8, 15 and 22. Treatment was continued until documented progressive disease, unacceptable toxicity, or the patient/physician determined it was not in the patient´s best interest to continue participation in the study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Melflufen (combined with orally administered dexamethasone) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Melflufen 40 mg was administered as a 30-minute central IV infusion on Day 1 of every 28-day cycle via a central catheter, which was inserted according to standard of care, prior to initiation of the first dose of melflufen.
Melflufen 20 mg was administered to subjects ≥ 75 years of age.

| | |
|---|---|
| Investigational medicinal product name | Dexamethasone (combined with once monthly melflufen) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection, Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dexamethasone 40 mg was self-administered orally once weekly on Days 1, 8, 15 and 22 of each 28-day cycle. Melflufen was also given to the patients on Day 1 of each cycle, in addition to intake of dexamethasone.
Dexamethasone 20 mg instead of 40 mg was used by subjects ≥ 75 years of age.
Overall in the trial, dexamethasone was administered in the pharmaceutical form of tablets (all countries) but in some cases it was administered as injections (US only).

| **Number of subjects in period 1** | Treatment |
|---|---|
| Started | 157 |
| Completed | 154 |
| Not completed | 3 |
| Lost to follow-up | 3 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall trial |
|---|---|

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 157 | 157 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 78 | 78 | |
| Adults 65 to < 75 years | 54 | 54 | |
| Adults ≥ 75 years | 25 | 25 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 68 | 68 | |
| Male | 89 | 89 | |

### Subject analysis sets

| Subject analysis set title | FAS |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

The Full Analysis Set (FAS) was defined as all patients who fulfilled all eligibility criteria at screening and prior to initiation of therapy. The FAS was used for summaries of disposition and all analyses of efficacy. All patients enrolled were included in the FAS.

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

Subject analysis set description:

The Safety Analysis Set was defined as all patients who received at least one dose of melflufen or dexamethasone. The Safety Analysis Set was used for all analyses of safety. In the current study the Safety Analysis Set consisted of the same number of patients as the FAS.

| Subject analysis set title | TCR-subgoup |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Patients refractory or intolerant to at least one proteasome inhibitor (PI), at least one immunomodulatory drug (IMiD), and at least one anti-CD38 monocloncal antibody, constituted the triple-class refractory (TCR) subpopulation.

| Reporting group values | FAS | Safety analysis set | TCR-subgoup |
|---|---|---|---|
| Number of subjects | 157 | 157 | 119 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 78 | 78 | 59 |
| Adults 65 to < 75 years | 54 | 54 | 41 |
| Adults ≥ 75 years | 25 | 25 | 19 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 68 | 68 | 49 |
| Male | 89 | 89 | 70 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Treatment |

Reporting group description:

This was a single-arm study and all enrolled subjects/patients were treated with 28-day cycles of therapy with melflufen on Day 1 and dexamethasone on Days 1, 8, 15 and 22. Treatment was continued until documented progressive disease, unacceptable toxicity, or the patient/physician determined it was not in the patient´s best interest to continue participation in the study.

| | |
|---|---|
| Subject analysis set title | FAS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The Full Analysis Set (FAS) was defined as all patients who fulfilled all eligibility criteria at screening and prior to initiation of therapy. The FAS was used for summaries of disposition and all analyses of efficacy. All patients enrolled were included in the FAS.

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

Subject analysis set description:

The Safety Analysis Set was defined as all patients who received at least one dose of melflufen or dexamethasone. The Safety Analysis Set was used for all analyses of safety. In the current study the Safety Analysis Set consisted of the same number of patients as the FAS.

| | |
|---|---|
| Subject analysis set title | TCR-subgoup |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Patients refractory or intolerant to at least one proteasome inhibitor (PI), at least one immunomodulatory drug (IMiD), and at least one anti-CD38 monoclonal antibody, constituted the triple-class refractory (TCR) subpopulation.

### Primary: Overall response rate

| | |
|---|---|
| End point title | Overall response rate[1] |

End point description:

The primary endpoint of this Phase 2 study was to measure the overall response rate (ORR) to treatment with melflufen in relapsed-refractory multiple myeloma (RRMM) patients. Overall response rate was defined as the proportion of patients for whom the best overall confirmed response was stringent complete response (sCR), complete response (CR), very good partial response (VGPR) or partial response (PR).
All tumor response and progression-dependent endpoints were assessed by the Investigator using the International Myeloma Working Group Uniform Response Criteria (IMWG-URC).

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

End point timeframe:

From the start of treatment up until confirmed response according to the IMWG response criteria.

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: This was a single arm study and hence no statistical analyses comparing groups were done. The 95 % exact confidence interval (Clopper-Pearson) for ORR is provided.

| End point values | Treatment | TCR-subgoup | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 157 | 119 | | |
| Units: Percentage of subjects evaluated | | | | |
| number (confidence interval 95%) | 33.8 (26.41 to 41.73) | 29.4 (21.42 to 38.46) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of response

| End point title | Duration of response |
|---|---|

End point description:

Duration of response (DOR) for patients who achieved a partial response (PR) or better was defined as the duration in months from first documentation of a confirmed response to first evidence of confirmed disease progression or death due to any cause.

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

End point timeframe:

For each patient, the "duration of response" was measured from the time of first confirmed response until the time of progression.

| **End point values** | Treatment | TCR-subgoup | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 157 | 119 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 6.70 (4.40 to 8.11) | 6.97 (3.75 to 9.79) | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The occurence of any AEs was monitored from intake of first dose of study medication up to 30 days after the last study drug administration.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Safety Analysis Set, overall population |
| Reporting group description: - | |
| Reporting group title | Safety Analysis Set, TCR-subgroup |

Reporting group description: -

| Serious adverse events | Safety Analysis Set, overall population | Safety Analysis Set, TCR-subgroup | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 88 / 157 (56.05%) | 70 / 119 (58.82%) | |
| number of deaths (all causes) | 130 | 105 | |
| number of deaths resulting from adverse events | 14 | 12 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 3 / 119 (2.52%) | |
| occurrences causally related to treatment / all | 2 / 3 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Plasma cell leukaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Refractory cytopenia with multilineage dysplasia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 5 / 119 (4.20%) | |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 3 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 3 / 119 (2.52%) | |
| occurrences causally related to treatment / all | 2 / 4 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse alveolar damage | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |

| | | | |
|---|---|---|---|
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 4 / 157 (2.55%) | 4 / 119 (3.36%) | |
| occurrences causally related to treatment / all | 6 / 6 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 157 (1.27%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural haematoma | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac amyloidosis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperammonaemic encephalopathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 119 (5.04%) | |
| occurrences causally related to treatment / all | 10 / 10 | 8 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 157 (3.18%) | 5 / 119 (4.20%) | |
| occurrences causally related to treatment / all | 6 / 6 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Methaemoglobinaemia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 2 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 4 / 157 (2.55%) | 4 / 119 (3.36%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephropathy | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Bone pain | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 16 / 157 (10.19%) | 8 / 119 (6.72%) | |
| occurrences causally related to treatment / all | 11 / 16 | 7 / 8 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 4 / 157 (2.55%) | 4 / 119 (3.36%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 3 / 119 (2.52%) | |
| occurrences causally related to treatment / all | 2 / 4 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 3 / 157 (1.91%) | 3 / 119 (2.52%) | |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Soft tissue infection | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 2 / 119 (1.68%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 157 (1.27%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis viral | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 119 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fungal sepsis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia influenzal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 4 / 157 (2.55%) | 4 / 119 (3.36%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Metabolic disorder | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 1 / 119 (0.84%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Safety Analysis Set, overall population | Safety Analysis Set, TCR-subgroup | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 157 / 157 (100.00%) | 119 / 119 (100.00%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 119 (5.04%) | |
| occurrences (all) | 12 | 10 | |

| | | | |
|---|---|---|---|
| Hypertension | | | |
| subjects affected / exposed | 6 / 157 (3.82%) | 6 / 119 (5.04%) | |
| occurrences (all) | 12 | 12 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 46 / 157 (29.30%) | 35 / 119 (29.41%) | |
| occurrences (all) | 74 | 56 | |
| Asthenia | | | |
| subjects affected / exposed | 45 / 157 (28.66%) | 30 / 119 (25.21%) | |
| occurrences (all) | 73 | 50 | |
| Pyrexia | | | |
| subjects affected / exposed | 39 / 157 (24.84%) | 28 / 119 (23.53%) | |
| occurrences (all) | 64 | 49 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 23 / 157 (14.65%) | 12 / 119 (10.08%) | |
| occurrences (all) | 25 | 14 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 29 / 157 (18.47%) | 21 / 119 (17.65%) | |
| occurrences (all) | 38 | 23 | |
| Dyspnoea | | | |
| subjects affected / exposed | 23 / 157 (14.65%) | 16 / 119 (13.45%) | |
| occurrences (all) | 27 | 20 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 16 / 157 (10.19%) | 11 / 119 (9.24%) | |
| occurrences (all) | 17 | 11 | |
| Epistaxis | | | |
| subjects affected / exposed | 14 / 157 (8.92%) | 12 / 119 (10.08%) | |
| occurrences (all) | 19 | 17 | |
| Productive cough | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 119 (5.04%) | |
| occurrences (all) | 10 | 7 | |
| Nasal congestion | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 6 / 119 (5.04%) | |
| occurrences (all) | 7 | 6 | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Insomnia | | | |
| subjects affected / exposed | 18 / 157 (11.46%) | 12 / 119 (10.08%) | |
| occurrences (all) | 22 | 13 | |
| Investigations | | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 45 / 157 (28.66%) | 35 / 119 (29.41%) | |
| occurrences (all) | 175 | 138 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 42 / 157 (26.75%) | 33 / 119 (27.73%) | |
| occurrences (all) | 210 | 166 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 40 / 157 (25.48%) | 33 / 119 (27.73%) | |
| occurrences (all) | 151 | 129 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 10 / 157 (6.37%) | 7 / 119 (5.88%) | |
| occurrences (all) | 17 | 13 | |
| Weight decreased | | | |
| subjects affected / exposed | 7 / 157 (4.46%) | 6 / 119 (5.04%) | |
| occurrences (all) | 7 | 6 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 17 / 157 (10.83%) | 13 / 119 (10.92%) | |
| occurrences (all) | 25 | 19 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 9 / 157 (5.73%) | 8 / 119 (6.72%) | |
| occurrences (all) | 12 | 11 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 21 / 157 (13.38%) | 17 / 119 (14.29%) | |
| occurrences (all) | 22 | 18 | |
| Dizziness | | | |
| subjects affected / exposed | 18 / 157 (11.46%) | 9 / 119 (7.56%) | |
| occurrences (all) | 22 | 13 | |
| Hypoaesthesia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 157 (4.46%) | 6 / 119 (5.04%) | |
| occurrences (all) | 8 | 7 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 113 / 157 (71.97%) | 78 / 119 (65.55%) | |
| occurrences (all) | 432 | 300 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 93 / 157 (59.24%) | 64 / 119 (53.78%) | |
| occurrences (all) | 628 | 415 | |
| Neutropenia | | | |
| subjects affected / exposed | 86 / 157 (54.78%) | 60 / 119 (50.42%) | |
| occurrences (all) | 549 | 374 | |
| Leukopenia | | | |
| subjects affected / exposed | 12 / 157 (7.64%) | 9 / 119 (7.56%) | |
| occurrences (all) | 53 | 41 | |
| Lymphopenia | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 119 (5.04%) | |
| occurrences (all) | 77 | 65 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 51 / 157 (32.48%) | 39 / 119 (32.77%) | |
| occurrences (all) | 67 | 53 | |
| Diarrhoea | | | |
| subjects affected / exposed | 43 / 157 (27.39%) | 28 / 119 (23.53%) | |
| occurrences (all) | 67 | 45 | |
| Constipation | | | |
| subjects affected / exposed | 24 / 157 (15.29%) | 20 / 119 (16.81%) | |
| occurrences (all) | 26 | 22 | |
| Vomiting | | | |
| subjects affected / exposed | 23 / 157 (14.65%) | 20 / 119 (16.81%) | |
| occurrences (all) | 30 | 26 | |
| Abdominal pain | | | |
| subjects affected / exposed | 10 / 157 (6.37%) | 6 / 119 (5.04%) | |
| occurrences (all) | 15 | 11 | |
| Dyspepsia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 157 (5.10%) | 6 / 119 (5.04%) | |
| occurrences (all) | 9 | 7 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 24 / 157 (15.29%) | 18 / 119 (15.13%) | |
| occurrences (all) | 26 | 19 | |
| Bone pain | | | |
| subjects affected / exposed | 21 / 157 (13.38%) | 15 / 119 (12.61%) | |
| occurrences (all) | 24 | 18 | |
| Arthralgia | | | |
| subjects affected / exposed | 19 / 157 (12.10%) | 13 / 119 (10.92%) | |
| occurrences (all) | 25 | 15 | |
| Back pain | | | |
| subjects affected / exposed | 19 / 157 (12.10%) | 11 / 119 (9.24%) | |
| occurrences (all) | 21 | 12 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 10 / 157 (6.37%) | 6 / 119 (5.04%) | |
| occurrences (all) | 13 | 7 | |
| Myalgia | | | |
| subjects affected / exposed | 10 / 157 (6.37%) | 9 / 119 (7.56%) | |
| occurrences (all) | 12 | 11 | |
| Muscular weakness | | | |
| subjects affected / exposed | 9 / 157 (5.73%) | 6 / 119 (5.04%) | |
| occurrences (all) | 9 | 6 | |
| Muscle spasms | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 4 / 119 (3.36%) | |
| occurrences (all) | 9 | 4 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 8 / 157 (5.10%) | 7 / 119 (5.88%) | |
| occurrences (all) | 9 | 7 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 24 / 157 (15.29%) | 19 / 119 (15.97%) | |
| occurrences (all) | 43 | 35 | |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 157 (3.82%) | 6 / 119 (5.04%) | |
| occurrences (all) | 7 | 7 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 23 / 157 (14.65%) | 16 / 119 (13.45%) | |
| occurrences (all) | 39 | 25 | |
| Decreased appetite | | | |
| subjects affected / exposed | 22 / 157 (14.01%) | 13 / 119 (10.92%) | |
| occurrences (all) | 25 | 16 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 17 / 157 (10.83%) | 11 / 119 (9.24%) | |
| occurrences (all) | 27 | 18 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 15 / 157 (9.55%) | 11 / 119 (9.24%) | |
| occurrences (all) | 28 | 18 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 14 / 157 (8.92%) | 10 / 119 (8.40%) | |
| occurrences (all) | 25 | 18 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 11 / 157 (7.01%) | 7 / 119 (5.88%) | |
| occurrences (all) | 15 | 7 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 31 May 2018 | The sample size was expanded to 150 patients and the two previously included patient populations were grouped into one patient population.<br>Initially, patients were either refractory to Pomalidomide or refractory to an anti-CD38 MAb. Once it was observed that more than 70% of patients were refractory to both and the original hypothesis was void, the two groups were merged into one with the possibility to be Pomalidomide and/or anti-CD38 MAb refractory. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/33296242