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 Units: Subjects			
Adults (18-64 years)	78	78	
Adults 65 to < 75 years	54	54	
Adults ≥ 75 years	25	25	
Gender categorical 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 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 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. 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