Clinical trial results:
A Phase II open-label, single-arm, multicenter trial of MP0250 plus bortezomib+dexamethasone in patients with refractory and relapsed multiple myeloma

Summary

EudraCT number	2016-002771-10
Trial protocol	DE PL DK AT CZ
Global end of trial date	13 January 2021

Results information

Result version number	v1 (current)
This version publication date	08 September 2021
First version publication date	08 September 2021

Trial information

Trial identification

Sponsor protocol code	MP0250-CP201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03136653
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Molecular Partners AG
Sponsor organisation address	Wagistrasse 14, Schlieren, Switzerland, 8952
Public contact	Clinical Trial Manager, Molecular Partners AG, info@molecularpartners.com
Scientific contact	Clinical Trial Manager, Molecular Partners AG, info@molecularpartners.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	11 May 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

There were 2 parts to this study. The main objectives for both parts were:
- Part 1: To estimate the efficacy of MP0250 plus bortezomib + dexamethasone, based on overall response rate (ORR), in patients with multiple myeloma (MM) who have received ≥2 lines of therapy, including bortezomib and an immunomodulatory drug (IMiD), and have shown no response to, or have progressed on the most recent treatment, or within 60 days of the most recent therapy.
- Part 2: To assess the preliminary efficacy of MP0250 in combination with bortezomib + dexamethasone in patients with refractory MM who have received ≥2 lines of therapy including a proteasome inhibitor (bortezomib, carfilzomib or both) and an IMiD (thalidomide, lenalidomide and/or pomalidomide) either alone or in combination and whose last line of therapy is either a bortezomib-or carfilzomib-based regimen.

Protection of trial subjects:

This study was conducted in accordance with the Note for Guidance on Good Clinical Practice (GCP) International Council for Harmonisation (ICH) Harmonised Tripartite Guideline E6 (R1)/Integrated Addendum E6 (R2); US Food and Drug Administration (FDA) Code of Federal Regulations (CFR) (Title 21 Parts 50, 56, 312), requirements for the conduct of clinical studies as provided in the EU Directive 2001/20/EC, the general guidelines indicated in the Declaration of Helsinki; and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2017
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	Poland: 12
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Italy: 6
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	22
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 24 research centers in Germany, Italy, Austria, Denmark, Poland, and Czechia from 11 May 2017 to 04 May 2020. The trial was terminated early on 04 May 2020 due to recent advances in the relapsed and refractory multiple myeloma (MM) treatment landscape.

Pre-assignment

Screening details:

Participants were enrolled into a lead-in phase (Part 1) for identification of the maximum tolerated dose (MTD) of MP0250. Part 2 enrolled additional participants for collection of additional safety and preliminary efficacy assessments.

Period 1

Period 1 title	Overall Study: Parts 1 & 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	8 mg/kg MP0250

Arm description:

Participants in Part 1 and Part 2 were administered 8 milligrams per kilogram of body weight (mg/kg) MP0250 as an intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 milligrams per square meter per dose (mg/m2/dose) as a subcutaneous (s.c.) injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.

Arm type	Experimental
Investigational medicinal product name	MP0250
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

8 mg/kg as an IV infusion via peripheral or central venous line

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.3 mg/m^2/dose as a s.c. injection

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg per oral (po) as an oral tablet

Arm title	12 mg/kg MP0250

Arm description:

Participants in Part 1 were administered 12 mg/kg of body weight MP0250 as an IV infusion Q3W on Day

1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 mg/m2/dose as a s.c. injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each
cycle.

Arm type	Experimental
Investigational medicinal product name	MP0250
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

12 mg/kg as an IV infusion via peripheral or central venous line

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.3 mg/m^2/dose as a s.c. injection

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg per oral (po) as an oral tablet

Number of subjects in period 1	8 mg/kg MP0250	12 mg/kg MP0250
Started	30	3
Completed	0	0
Not completed	30	3
Discontinued	30	3

Baseline characteristics

Reporting groups	
Reporting group title	8 mg/kg MP0250
Reporting group description:	
Participants in Part 1 and Part 2 were administered 8 milligrams per kilogram of body weight (mg/kg) MP0250 as an intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 milligrams per square meter per dose (mg/m2/dose) as a subcutaneous (s.c.) injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.	
Reporting group title	12 mg/kg MP0250
Reporting group description:	
Participants in Part 1 were administered 12 mg/kg of body weight MP0250 as an IV infusion Q3W on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 mg/m2/dose as a s.c. injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.	

Reporting group values	8 mg/kg MP0250	12 mg/kg MP0250	Total
Number of subjects	30	3	33
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	60.4	55.7	
standard deviation	± 8.62	± 3.21	-
Gender categorical Units: Subjects			
Female	16	2	18
Male	14	1	15
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	30	3	33
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	8 mg/kg MP0250

Reporting group description:

Participants in Part 1 and Part 2 were administered 8 milligrams per kilogram of body weight (mg/kg) MP0250 as an intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 milligrams per square meter per dose (mg/m2/dose) as a subcutaneous (s.c.) injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.

Reporting group title	12 mg/kg MP0250

Reporting group description:

Participants in Part 1 were administered 12 mg/kg of body weight MP0250 as an IV infusion Q3W on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 mg/m2/dose as a s.c. injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each
cycle.

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1][2]

End point description:

ORR defined as the percentage of participants achieving a stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) per the International Myeloma Working Group (IMWG) as determined by the Investigator.

End point type	Primary

End point timeframe:

Day 1 until disease progression, death or discontinuation plus 7 days

Notes:

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

[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: The Full Analysis Set (FAS) for efficacy included all participants who were treated with 8 mg/kg MP0250 in Parts 1 and 2 and had measurable disease at baseline and completed at least 1 assessment of response.

End point values	8 mg/kg MP0250			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: percentage of participants				
number (confidence interval 95%)	32.1 (17.9 to 50.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A TEAE was any AE occurring or worsening on or after the first dose of study treatment, up to 28 days after the last dose of MP0250.

Severity of TEAEs were assessed based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03, grades 3 or greater:
• Grade 3: severe
• Grade 4: life-threatening
• Grade 5: fatal

Clinically significant changes from baseline in laboratory analytes, vital signs and electrocardiogram (ECG) findings were also considered TEAEs.

End point type	Secondary

End point timeframe:

Day 1 until 28 days after the last treatment

End point values	8 mg/kg MP0250	12 mg/kg MP0250		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	3		
Units: Participants				
Any TEAE	28	3		
Any Grade >=3 TEAE	26	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With a Positive Anti-drug Antibody (ADA) Result

End point title	Number of Participants With a Positive Anti-drug Antibody (ADA) Result

End point description:

ADA tests were performed at baseline, during study treatment, at the end of study treatment and at follow up.

End point type	Secondary

End point timeframe:

Day 1 until disease progression, death or discontinuation

End point values	8 mg/kg MP0250	12 mg/kg MP0250		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	3		
Units: Participants				
Baseline	2	1		
During study treatment	5	0		
End of treatment	0	0		
Follow-up	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Average Range of ADA Titer in Participants who Tested Positive for ADA After Treatment

End point title	Average Range of ADA Titer in Participants who Tested Positive for ADA After Treatment

End point description:

Serum samples were collected to analyze the titers of antibodies against MP0250. Values of 99999 indicate that no values could be calculated.

End point type	Secondary

End point timeframe:

Day 1 until disease progression, death or discontinuation

End point values	8 mg/kg MP0250	12 mg/kg MP0250		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0[3]		
Units: titer				
arithmetic mean (standard deviation)				
Lower value	99999 (± 99999)	()		
Higher value	99999 (± 99999)	()		

Notes:

[3] - There were no participants who tested positive for ADA post-treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time-course of Anti-drug Antibodies (ADAs)

End point title	Time-course of Anti-drug Antibodies (ADAs)

End point description:

The time to onset of ADA was defined as time (months) between the first day of study treatment and date of first detection of ADA.

End point type	Secondary

End point timeframe:

Day 1 until disease progression, death or discontinuation plus 7 days

End point values	8 mg/kg MP0250	12 mg/kg MP0250		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0[4]		
Units: months				
median (full range (min-max))	0.71 (0.7 to 7.9)	(to)		

Notes:

[4] - No participants tested positive for ADA after treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[5]

End point description:

PFS was defined as the time in days from the first dose of MP0250 to progressive disease or death from myeloma. Deaths from other causes were censored. PFS was summarized using Kaplan-Meier (K-M) methodology.

End point type	Secondary

End point timeframe:

Day 1 until disease progression or death from myeloma

Notes:

[5] - 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: The Full Analysis Set (FAS) for efficacy included all participants who were treated with 8 mg/kg MP0250 in Parts 1 and 2 and had measurable disease at baseline and completed at least 1 assessment of response.

End point values	8 mg/kg MP0250			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: days				
median (confidence interval 95%)	126.0 (58.0 to 213.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)[6]

End point description:

DOR was defined as the time from the earliest date of documented response (≥PR per the IMWG) to the

first occurrence of disease progression or death from myeloma (with deaths from other causes censored). All responders were used for the response duration analysis, which was summarized using K-M estimates.

The value of 99999 indicates that the upper limit could not be calculated.

End point type	Secondary

End point timeframe:

Day 1 until disease progression, death or discontinuation plus 7 days

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Full Analysis Set (FAS) for efficacy included all participants who were treated with 8 mg/kg MP0250 in Parts 1 and 2.

End point values	8 mg/kg MP0250			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: days				
median (confidence interval 95%)	238.5 (151.0 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events: Day 1 until 28 days after the last treatment; Mortality: Day 1 until 30 days after the last treatment

Adverse event reporting additional description:

All-cause mortality is reported for all participants who enrolled in the study (n=30 for 8 mg/kg; n=3 for 12 mg/kg). Serious adverse events and other adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2 (n=28 for 8 mg/kg; n=3 for 12 mg/kg).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	8 mg/kg MP0250

Reporting group description:

Participants in Part 1 and Part 2 were administered 8 mg/kg MP0250 as an IV infusion Q3W on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 milligrams per square meter mg/m2/dose as a s.c. injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.

Reporting group title	12 mg/kg MP0250

Reporting group description:

Participants in Part 1 were administered 12 mg/kg of body weight MP0250 as an IV infusion Q3W on Day 1 of each cycle (1 cycle was 21 days) in combination with bortezomib 1.3 mg/m2/dose as a s.c. injection on Days 1, 4, 8, and 11 of each cycle and 20 mg dexamethasone as oral tablets on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each cycle.

Serious adverse events	8 mg/kg MP0250	12 mg/kg MP0250	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 30 (46.67%)	2 / 3 (66.67%)	
number of deaths (all causes)	8	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed[1]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed[2]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed[3]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed[4]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed[5]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed[6]	1 / 28 (3.57%)	0 / 3 (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			
Thrombocytopenia			
subjects affected / exposed[7]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed[8]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed[9]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			

subjects affected / exposed[10]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed[11]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed[12]	1 / 28 (3.57%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Proteinuria			
subjects affected / exposed[13]	1 / 28 (3.57%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed[14]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed[15]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device issue			
subjects affected / exposed[16]	1 / 28 (3.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

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

Non-serious adverse events	8 mg/kg MP0250	12 mg/kg MP0250	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 30 (93.33%)	3 / 3 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed[17]	18 / 28 (64.29%)	1 / 3 (33.33%)	
occurrences (all)	65	1	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed[18]	7 / 28 (25.00%)	2 / 3 (66.67%)	
occurrences (all)	8	3	
Fatigue			
subjects affected / exposed[19]	7 / 28 (25.00%)	1 / 3 (33.33%)	
occurrences (all)	10	1	
Asthenia			
subjects affected / exposed[20]	3 / 28 (10.71%)	2 / 3 (66.67%)	
occurrences (all)	8	2	
Chest pain			
subjects affected / exposed[21]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Face oedema			
subjects affected / exposed[22]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed[23]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Mucosal inflammation			
subjects affected / exposed[24]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Pain			
subjects affected / exposed[25]	1 / 28 (3.57%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 3 (33.33%)	
occurrences (all)	2	2	
Oedema			

subjects affected / exposed[26]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vulvovaginal pruritus			
subjects affected / exposed[27]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed[28]	4 / 28 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	10	5	
Dysphonia			
subjects affected / exposed[29]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Dyspnoea			
subjects affected / exposed[30]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed[31]	4 / 28 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Restlessness			
subjects affected / exposed[32]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Mood altered			
subjects affected / exposed[33]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Sleep disorder			
subjects affected / exposed[34]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Investigations			
Blood creatinine increased			
subjects affected / exposed[35]	4 / 28 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	6	1	
Gamma-glutamyltransferase increased			

subjects affected / exposed[36]	5 / 28 (17.86%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Platelet count decreased			
subjects affected / exposed[37]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Alanine aminotransferase increased			
subjects affected / exposed[38]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Aspartate aminotransferase increased			
subjects affected / exposed[39]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Lipase increased			
subjects affected / exposed[40]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
White blood cell count decreased			
subjects affected / exposed[41]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Lymphocyte count decreased			
subjects affected / exposed[42]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed[43]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Polyneuropathy			
subjects affected / exposed[44]	6 / 28 (21.43%)	0 / 3 (0.00%)	
occurrences (all)	10	0	
Headache			
subjects affected / exposed[45]	4 / 28 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	4	2	
Neuropathy peripheral			
subjects affected / exposed[46]	3 / 28 (10.71%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Dizziness			

subjects affected / exposed[47]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Sciatica			
subjects affected / exposed[48]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed[49]	0 / 28 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed[50]	13 / 28 (46.43%)	3 / 3 (100.00%)	
occurrences (all)	44	13	
Anaemia			
subjects affected / exposed[51]	5 / 28 (17.86%)	2 / 3 (66.67%)	
occurrences (all)	16	8	
Lymphopenia			
subjects affected / exposed[52]	4 / 28 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	35	0	
Leukopenia			
subjects affected / exposed[53]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Neutropenia			
subjects affected / exposed[54]	2 / 28 (7.14%)	1 / 3 (33.33%)	
occurrences (all)	2	4	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed[55]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Eye disorders			
Cataract			
subjects affected / exposed[56]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[57]	8 / 28 (28.57%)	1 / 3 (33.33%)	
occurrences (all)	15	1	
Nausea			

subjects affected / exposed[58]	5 / 28 (17.86%)	1 / 3 (33.33%)	
occurrences (all)	6	2	
Abdominal pain upper			
subjects affected / exposed[59]	4 / 28 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Constipation			
subjects affected / exposed[60]	3 / 28 (10.71%)	1 / 3 (33.33%)	
occurrences (all)	3	2	
Abdominal pain			
subjects affected / exposed[61]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Vomiting			
subjects affected / exposed[62]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed[63]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed[64]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Skin ulcer			
subjects affected / exposed[65]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed[66]	8 / 28 (28.57%)	2 / 3 (66.67%)	
occurrences (all)	10	2	
Albuminuria			
subjects affected / exposed[67]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Oliguria			
subjects affected / exposed[68]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed[69]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal chest pain			
subjects affected / exposed[70]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Muscle spasms			
subjects affected / exposed[71]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed[72]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	3	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed[73]	9 / 28 (32.14%)	0 / 3 (0.00%)	
occurrences (all)	13	0	
Respiratory tract infection			
subjects affected / exposed[74]	3 / 28 (10.71%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Cystitis			
subjects affected / exposed[75]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	5	0	
Periodontitis			
subjects affected / exposed[76]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Pneumonia			
subjects affected / exposed[77]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed[78]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Diverticulitis			
subjects affected / exposed[79]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Herpes Zoster			

subjects affected / exposed[80]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Fungal skin infection			
subjects affected / exposed[81]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed[82]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed[83]	0 / 28 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed[84]	3 / 28 (10.71%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Decreased appetite			
subjects affected / exposed[85]	3 / 28 (10.71%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Hypercalcaemia			
subjects affected / exposed[86]	0 / 28 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	3	
Hypercholesterolaemia			
subjects affected / exposed[87]	2 / 28 (7.14%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hypocalcaemia			
subjects affected / exposed[88]	1 / 28 (3.57%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed[89]	0 / 28 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	

Notes:

[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[18] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[19] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[20] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[21] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[22] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[23] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[24] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[25] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[26] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[27] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[28] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[29] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[30] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[31] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[32] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[33] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.
[34] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[35] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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MP0250 in either Part 1 or Part 2.

[36] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[37] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[38] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[39] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[42] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[43] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[44] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[45] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[46] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[48] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[49] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[69] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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MP0250 in either Part 1 or Part 2.

[86] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[87] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[88] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

[89] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events are reported for all participants who received at least 1 dose of MP0250 in either Part 1 or Part 2.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2017	• The exclusion criteria were modified. • Screening assessment details were modified. • An additional follow-up visit for safety was added to capture any AE after end of study (EoS) and end of the follow-up period. • Criteria for the initiation of a New Cycle of Treatment were added. • Treatment Dose Modification/Treatment Delay Recommendations section was modified in accordance with Investigator Brochure (IB) V3.0. In addition, further instructions were added for MP0250 and dexamethasone aiming to facilitate treatment and dose modifications.
19 December 2018	• Primary objective for Part 2 under the new participant population was added describing that MM subjects who had received ≥2 lines of therapy, including bortezomib and IMiD, and had shown no response or progressed on most recent therapy and had received most recent therapy (must be a bortezomib- or carfilzomib-based regimen) were to be assessed for ORR. • Study endpoints were modified: Secondary safety endpoint - to include changes from baseline in selected laboratory analytes to further determine the safety profile of MP0250. Secondary efficacy endpoint – to enable correct assessment of DOR from the first observation of PR or better until disease progression or death from myeloma according to the International Myeloma Workshop Consensus Panel 1. • The number of participants to be enrolled was updated. • Baseline disease assessments were modified to include all available imaging modalities considered standard of care in relapse/refractory multiple myeloma (RRMM). • Overall Survival (OS) was modified to include OS visit after completion of follow-up period. Survival follow-up criteria were added. • MP0250 dosing instructions were modified from 3 hours to 1 hour infusion followed by 25 mL 0.9% NaCl flush volume. • Dexamethasone dosing instructions were modified for participants aged ≥75 years or considered frail by Investigator; it was recommended that this group of participants received reduced dexamethasone to avoid unnecessary toxicity. • Dose modifications for MP0250 were modified since it had been demonstrated that the 12 mg/kg Q3W dose was insufficiently tolerated in Part 1. • For Part 2 of the study, the dose-escalation committee (DEC) would review safety in the event of any unexpected safety signals.

30 July 2020	• To reduce the intensity of study visits for ongoing participants, the Day 15 study visit of each cycle would no longer be performed. • Analyses required for efficacy assessment and evaluation of primary and secondary endpoints would no longer be performed by central laboratory. • Bone Marrow (BM) aspirate/biopsy, and assessment of soft tissue involvement were no longer required. • Efficacy assessment was to be based on the local laboratory results; these data were not to be used for evaluation of primary and secondary endpoints but to assess whether the participant was responding and if a new cycle of study treatment was to be initiated. • For participants who were discontinued from study treatment, no further efficacy assessments would be done following the end of treatment (EOT) visit. • As the study was at an early stage and due to the consequential limited available data, survival data would no longer be collected. • No further analyses of cytokine biomarker panel. • No further fluorescence in-situ hybridization (FISH) analyses would be performed. • Pharmacokinetics (PK) would be collected only on Day 1 of each cycle and at the EOT visit. • EoS would occur 3 months after the last ongoing participant discontinued from study treatment (3-month follow-up visit), or death, withdrawal of consent, or lost to follow-up, whichever occurred earlier. • The final analyses would occur when the last ongoing participant had switched to Protocol V4.0 or discontinued study treatment (regardless of the reason), whichever occurred first. For the primary analyses, the FAS that includes participants enrolled in Part 1 and Part 2 would be used. • No further DEC data review meetings were anticipated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

It was planned that up to 54 participants would enroll. However, recruitment was stopped by Sponsor decision on 04 May 2020, before this was achieved, as the study design no longer supported recent advances in the RRMM treatment landscape.

Notes: