Clinical trial results:
A Phase 2 Multi-Arm Study of Magrolimab Combinations in Patients with Relapsed/Refractory Multiple Myeloma

Summary

EudraCT number	2021-001798-21
Trial protocol	CZ
Global end of trial date	25 April 2024

Results information

Result version number	v1 (current)
This version publication date	01 May 2025
First version publication date	01 May 2025

Trial information

Trial identification

Sponsor protocol code	GS-US-558-5915

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04892446
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 April 2024
Global end of trial reached?	Yes
Global end of trial date	25 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The goal of this clinical study was to learn more about the safety and dosing of the study drug, magrolimab, in combination with other anticancer therapies in participants with relapsed/refractory multiple myeloma.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	36
EEA total number of subjects	9

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)	0
From 65 to 84 years	19
85 years and over	17

Subject disposition

Recruitment

Recruitment details:

43 participants were screened.
As all participants were dosed with same dose of magrolimab, per prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined except for dose limiting toxicity outcome measure, for which data was collected only in Safety Run-in Cohorts.

Pre-assignment

Screening details:

Participants were enrolled at study sites in the United States, Czech Republic, and Canada. Magrolimab in combination with bortezomib and dexamethasone cohort was not initiated due to early closure of study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Magrolimab+Daratumumab

Arm description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an immunomodulatory drug (IMiD) and a proteasome inhibitor (PI) received magrolimab intravenously (IV) 1 milligrams per kilogram (mg/kg) on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received daratumumab 1800 mg subcutaneously (SC) or 16 mg/kg IV on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2; and Days 1, 15 (every 2 weeks) until Cycle 6 (total of 8 doses) followed by Day 1 (every 4 weeks) for subsequent cycles. (Cycle 1=35 days, All other Cycles=28 days).

Arm type	Experimental
Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Administered either subcutaneously or intravenously

Investigational medicinal product name	Magrolimab
Investigational medicinal product code	
Other name	GS-4721
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously

Arm title	Magrolimab+Pomalidomide+Dexamethasone

Arm description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received pomalidomide orally 4 mg on Days 1 to 21 (daily) of Cycle 1 and onward and dexamethasone orally 40 mg on Days 1, 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Administered orally

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

Dosage and administration details:

Administered orally

Investigational medicinal product name	Magrolimab
Investigational medicinal product code	
Other name	GS-4721
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously

Arm title	Magrolimab+Carfilzomib+Dexamethasone

Arm description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received carfilzomib IV 20 milligrams per square meter (mg/m^2) on Days 8, 15, 22 of Cycle 1; Days 1, 8, 15 of Cycle 2 and onward (if the carfilzomib starting dose of 20 mg/m^2 was tolerated after Cycle 1, Day 8, the dose was escalated to 70 mg/m^2 on Cycle 1, Day 15 and thereafter) and dexamethasone orally or IV 40 mg on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycles 2 to 9 and then Days 1, 8, 15 from Cycle 10 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Arm type	Experimental
Investigational medicinal product name	Carfilzomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously

Investigational medicinal product name	Magrolimab
Investigational medicinal product code	
Other name	GS-4721
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously

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

Dosage and administration details:

Administered orally

Number of subjects in period 1[1]	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone
Started	14	10	11
Completed	7	5	8
Not completed	7	5	3
Death	4	4	-
Study terminated by sponsor	-	-	2
Withdrew consent	3	-	1
Investigator's discretion	-	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One participant was enrolled but did not receive study drug in Magrolimab+Daratumumab cohort.

Baseline characteristics

Reporting groups	
Reporting group title	Magrolimab+Daratumumab
Reporting group description:	
Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an immunomodulatory drug (IMiD) and a proteasome inhibitor (PI) received magrolimab intravenously (IV) 1 milligrams per kilogram (mg/kg) on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards. Participants also received daratumumab 1800 mg subcutaneously (SC) or 16 mg/kg IV on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2; and Days 1, 15 (every 2 weeks) until Cycle 6 (total of 8 doses) followed by Day 1 (every 4 weeks) for subsequent cycles. (Cycle 1=35 days, All other Cycles=28 days).	
Reporting group title	Magrolimab+Pomalidomide+Dexamethasone
Reporting group description:	
Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards. Participants also received pomalidomide orally 4 mg on Days 1 to 21 (daily) of Cycle 1 and onward and dexamethasone orally 40 mg on Days 1, 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2 and onward. (Cycle 1=35 days, All other Cycles=28 days).	
Reporting group title	Magrolimab+Carfilzomib+Dexamethasone
Reporting group description:	
Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards. Participants also received carfilzomib IV 20 milligrams per square meter (mg/m^2) on Days 8, 15, 22 of Cycle 1; Days 1, 8, 15 of Cycle 2 and onward (if the carfilzomib starting dose of 20 mg/m^2 was tolerated after Cycle 1, Day 8, the dose was escalated to 70 mg/m^2 on Cycle 1, Day 15 and thereafter) and dexamethasone orally or IV 40 mg on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycles 2 to 9 and then Days 1, 8, 15 from Cycle 10 and onward. (Cycle 1=35 days, All other Cycles=28 days).	

Reporting group values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone
Number of subjects	14	10	11
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65	66	68
standard deviation	± 9.5	± 10.2	± 8.0
Gender categorical Units: Subjects			
Female	10	2	5
Male	4	8	6
Race Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	1	0	0
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	1	1	1
White	11	9	10
More than one race	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	14	10	11
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	35		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	17		
Male	18		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	1		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	3		
White	30		
More than one race	0		
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	35		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Magrolimab+Daratumumab

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an immunomodulatory drug (IMiD) and a proteasome inhibitor (PI) received magrolimab intravenously (IV) 1 milligrams per kilogram (mg/kg) on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received daratumumab 1800 mg subcutaneously (SC) or 16 mg/kg IV on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2; and Days 1, 15 (every 2 weeks) until Cycle 6 (total of 8 doses) followed by Day 1 (every 4 weeks) for subsequent cycles. (Cycle 1=35 days, All other Cycles=28 days).

Reporting group title	Magrolimab+Pomalidomide+Dexamethasone

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received pomalidomide orally 4 mg on Days 1 to 21 (daily) of Cycle 1 and onward and dexamethasone orally 40 mg on Days 1, 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Reporting group title	Magrolimab+Carfilzomib+Dexamethasone

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.

Participants also received carfilzomib IV 20 milligrams per square meter (mg/m^2) on Days 8, 15, 22 of Cycle 1; Days 1, 8, 15 of Cycle 2 and onward (if the carfilzomib starting dose of 20 mg/m^2 was tolerated after Cycle 1, Day 8, the dose was escalated to 70 mg/m^2 on Cycle 1, Day 15 and thereafter) and dexamethasone orally or IV 40 mg on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycles 2 to 9 and then Days 1, 8, 15 from Cycle 10 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Primary: Percentage of Participants Experiencing Dose-limiting Toxicities (DLTs) According to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0

End point title	Percentage of Participants Experiencing Dose-limiting Toxicities (DLTs) According to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0[1]

End point description:

A DLT is defined as any Grade 3 or higher hematologic toxicity or Grade 3 or higher nonhematologic toxicity, that has worsened in severity from pretreatment baseline during the DLT assessment period and, in the opinion of the investigator, the adverse event (AE) is at least possibly related to magrolimab. The DLT-Evaluable Analysis Set included all participants in the Safety Analysis Set who are enrolled in the Safety Run-in cohorts and fulfil the criteria for evaluation for DLT specified in the protocol. As all participants were dosed with same dose of magrolimab, per prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined except for dose limiting toxicity endpoint, for which data was collected only in Safety Run-in Cohorts.
Percentages are rounded off.

End point type	Primary

End point timeframe:

Up to 35 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: As prespecified only descriptive analysis was planned.

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: percentage of participants				
number (not applicable)	16.7	16.7	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Treatment-emergent Adverse Events (TEAE's) According to the NCI CTCAE Version 5.0

End point title	Percentage of Participants Experiencing Treatment-emergent Adverse Events (TEAE's) According to the NCI CTCAE Version 5.0[2]

End point description:

An AE is any untoward medical occurrence in a clinical study participant administered a study drug that does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a study drug, whether or not the AE is considered related to the study drug. A treatment-emergent AE was defined as any AE that began on or after the date of first dose of any study drug up to the date of last dose of any study drug plus 70 days. The Safety Analysis Set included all participants who received at least 1 dose of study treatment with treatment group designated according to the actual treatment received.
As all participants were dosed with same dose of magrolimab, per prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined for all 3 arms.

End point type	Primary

End point timeframe:

Up to 1.3 years plus 70 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As prespecified only descriptive analysis was planned.

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	10	11	
Units: percentage of participants				
number (not applicable)	100	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Treatment-emergent Laboratory Abnormalities According to the NCI CTCAE Version 5.0

End point title	Percentage of Participants Experiencing Treatment-emergent Laboratory Abnormalities According to the NCI CTCAE Version 5.0[3]

End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and included the date of last dose of study drug plus 70 days for participants who permanently discontinued study drug, or the day before initiation of new anticancer therapy including stem cell transplant (SCT) (whichever was earlier). If the relevant baseline laboratory value was missing, any abnormality of at least Grade 1 observed within the time frame specified above was considered treatment emergent. Participants in the Safety Analysis Set were analysed. As all participants were dosed with same dose of magrolimab, per prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined for all 3 arms. Percentages are rounded off.

End point type	Primary

End point timeframe:

Up to 1.3 years plus 70 days

Notes:

[3] - 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: As prespecified only descriptive analysis was planned.

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	10	11	
Units: percentage of participants				
number (not applicable)				
Hematology: Any Grade 1 or Higher	92.9	100	100	
Chemistry: Any Grade 1 or Higher	92.9	100	100	

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[4]

End point description:

ORR=percentage of participants who achieve confirmed stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR), as assessed by investigator per International Myeloma Working Group (IMWG) 2016 criteria. CR=negative immunofixation on serum and urine & disappearance of any soft tissue plasmacytomas &< 5% plasma cells in bone marrow (BM) aspirates; sCR=CR as above plus normal serum free light-chain (FLC) assay ratio & absence of clonal cells in BM biopsy by immunohistochemistry; VGPR=serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥ 90% reduction in serum M-protein plus urine M-protein <100 mg/24 h; PR=≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg/24 h. The Full Analysis Set included all participants who took ≥ 1 dose of study drugs with arm designated according to the planned treatment at enrollment. Percentages are rounded off.

End point type	Primary

End point timeframe:

Up to 1.5 years

Notes:

[4] - 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: As prespecified only descriptive analysis was planned.

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	10	11	
Units: percentage of participants				
number (confidence interval 95%)	14.3 (1.8 to 42.8)	20.0 (2.5 to 55.6)	36.4 (10.9 to 69.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Magrolimab

End point title	Serum Concentration of Magrolimab

End point description:

Arm 1: Magrolimab+Daratumumab; Arm 2: Magrolimab+Pomalidomide+Dexamethasone; Arm 3: Magrolimab+Carfilzomib+Dexamethasone; D=Day.
The PK Analysis Set included all participants who received ≥ 1 dose of magro and had ≥ 1 measurable posttreatment serum concentration of magrolimab. Participants with available data were analyzed.
As all participants were dosed with same dose of magrolimab, per prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined for all 3 arms.
9999: Mean and standard deviation were not calculable as the values were below the limit of quantitation.
99999: Standard deviation was not calculable due to less than 3 participants available for analysis.
999999: As no sample was collected, mean and standard deviation were not calculated.

End point type	Secondary

End point timeframe:

Arm 1, 2, 3: Predose: Days 1 and 22 of Cycle 1, Day 1 of Cycles 2, 3, 4, 5, 7, and on last sample collection day (anytime; up to Day 358); Arm 1 and 3: Predose: Day 1 of Cycles 10 and 13

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: ng/mL				
arithmetic mean (standard deviation)				
Predose: Cycle 1 D 1 N=10,10,10	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	
Predose: Cycle 1 D 22 N=8,8,7	435000 (± 245000)	303000 (± 182000)	421000 (± 115000)	
Predose: Cycle 2 D 1 N=7,5,8	621000 (± 233000)	713000 (± 293000)	675000 (± 274000)	
Predose: Cycle 3 D 1 N=4,6,8	853000 (± 399000)	739000 (± 365000)	847000 (± 238000)	

Predose: Cycle 4 D 1 N=2,1,2	694000 (± 82700)	5540 (± 99999)	459000 (± 161000)	
Predose: Cycle 5 D 1 N=3,5,5	517000 (± 186000)	373000 (± 142000)	448000 (± 90700)	
Predose: Cycle 7 D 1 N=1,3,4	332000 (± 99999)	307000 (± 153000)	376000 (± 140000)	
Predose: Cycle 10 D 1 N=1,0,2	336000 (± 99999)	999999 (± 999999)	361000 (± 345000)	
Predose: Cycle 13 D 1 N=1,0,1	295000 (± 99999)	999999 (± 999999)	624000 (± 99999)	
Anytime: Up to D 358 N=9,6,2	445000 (± 337000)	179000 (± 131000)	86000 (± 34000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DoR: earliest date of sCR, CR, VGPR, or PR, until earliest date of documented progression disease (PD), documented relapse, or death from any cause, whichever occurred first. sCR, CR, VGPR, or PR as defined in endpoint#4. PD: increase of 25% from lowest confirmed response value/appearance of new lesion, ≥ 50% increase in sum of products of 2 longest perpendicular diameters of >1 lesion, or ≥ 50% increase in longest diameter of previous lesion >1 cm in short axis; ≥ 50% increase in circulating plasma cells. Relapse=direct indicators of increasing disease/increase in size of existing or new soft tissue plasmacytomas or bone lesions/hypercalcemia (> 11 mg/dL)/decrease in hemoglobin of ≥ 2 g/dL/rise in serum creatinine by 2mg/dL/hyperviscosity. Participants in FAS who had objective response were analysed. 9999:Median, lower & upper limit (UL) of CI not estimable due to low number of participants with event;99999:Median & UL were not estimable due to low number of participants with events.

End point type	Secondary

End point timeframe:

Up to 1.5 years

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	4	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	99999 (3.9 to 99999)	9999 (9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Positive Anti-magrolimab Antibodies

End point title	Percentage of Participants With Positive Anti-magrolimab Antibodies

End point description:

Percentage of participants who had treatment induced or treatment-boosted anti-drug antibody (ADA) based on participants who had non-missing baseline ADA sample and at least one post-treatment ADA result reported in Immunogenicity Analysis Set. Treatment-Induced ADA: participants who had negative baseline ADA sample and at least one positive post-treatment ADA sample based on participants who had both non-missing baseline and at least one post-treatment ADA result reported. Treatment-Boosted ADA: participants who had positive baseline ADA sample and at least one positive post-treatment ADA sample and the (max titer of the posttreatment ADA)/(titer of baseline ADA) >= 4. The Immunogenicity Analysis Set included all enrolled participants who received at least 1 dose of magrolimab and have at least 1 evaluable anti-magrolimab antibody test result.
As prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined for all 3 arms.

End point type	Secondary

End point timeframe:

Up to Day 358

End point values	Magrolimab+Daratumumab	Magrolimab+Pomalidomide+Dexamethasone	Magrolimab+Carfilzomib+Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	10	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality (ACM): Up to 1.5 years; Adverse events (AE): Up to 1.3 years plus 70 days

Adverse event reporting additional description:

ACM: The All Enrolled Analysis Set included all participants who received a study patient identification number after screening. AE: Participants in the Safety Analysis Set were analyzed. As prespecified analysis, data for Safety Run-in and corresponding Dose-expansion cohorts were combined for all 3 arms.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Magrolimab+Daratumumab

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/ kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.
Participants also received daratumumab 1800 mg SC or 16 mg/kg IV on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2; and Days 1, 15 (every 2 weeks) until Cycle 6 (total of 8 doses) followed by Day 1 (every 4 weeks) for subsequent cycles. (Cycle 1=35 days, All other Cycles=28 days).

Reporting group title	Magrolimab+Carfilzomib +Dexamethasone

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/ kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.
Participants also received carfilzomib IV 20 mg/m^2 on Days 8, 15, 22 of Cycle 1; Days 1, 8, 15 of Cycle 2 and onward (if the carfilzomib starting dose of 20 mg/m^2 was tolerated after Cycle 1, Day 8, the dose was escalated to 70 mg/m^2 on Cycle 1, Day 15 and thereafter) and dexamethasone orally or IV 40 mg on Days 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycles 2 to 9 and then Days 1, 8, 15 from Cycle 10 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Reporting group title	Magrolimab+Pomalidomide +Dexamethasone

Reporting group description:

Participants in Safety Run-in and Dose-expansion period with relapsed/refractory multiple myeloma who have had 3 or more prior therapies including an IMiD and a PI received magrolimab IV 1 mg/kg on Day 1 and 30 mg/ kg on Days 8, 15, 22, 29 of Cycle 1; 30 mg/kg every week on Days 1, 8, 15, 22 of Cycle 2; 30 mg/kg on Days 1, 15 from Cycle 3 onwards.
Participants also received pomalidomide orally 4 mg on Days 1 to 21 (daily) of Cycle 1 and onward and dexamethasone orally 40 mg on Days 1, 8, 15, 22, 29 of Cycle 1; Days 1, 8, 15, 22 of Cycle 2 and onward. (Cycle 1=35 days, All other Cycles=28 days).

Serious adverse events	Magrolimab+Daratumumab	Magrolimab+Carfilzomib +Dexamethasone	Magrolimab+Pomalidomide +Dexamethasone
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 14 (35.71%)	4 / 11 (36.36%)	5 / 10 (50.00%)
number of deaths (all causes)	4	0	4
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Assisted suicide			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pathological fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Magrolimab+Daratumumab	Magrolimab+Carfilzomib +Dexamethasone	Magrolimab+Pomalidomide +Dexamethasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	11 / 11 (100.00%)	10 / 10 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	2	1	2
Hypotension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 14 (42.86%)	6 / 11 (54.55%)	3 / 10 (30.00%)
occurrences (all)	8	6	3
Oedema peripheral			
subjects affected / exposed	1 / 14 (7.14%)	3 / 11 (27.27%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Pyrexia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	3	2	1
Chills			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Influenza like illness			

subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 14 (21.43%)	4 / 11 (36.36%)	3 / 10 (30.00%)
occurrences (all)	3	5	3
Cough			
subjects affected / exposed	1 / 14 (7.14%)	4 / 11 (36.36%)	2 / 10 (20.00%)
occurrences (all)	1	5	2
Nasal congestion			
subjects affected / exposed	3 / 14 (21.43%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	4	1	1
Dysphonia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Upper-airway cough syndrome			

subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Wheezing			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Dyspnoea exertional			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	1	1	3
Product issues			
Device breakage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	2 / 14 (14.29%)	7 / 11 (63.64%)	3 / 10 (30.00%)
occurrences (all)	2	8	3
Neutrophil count decreased			
subjects affected / exposed	2 / 14 (14.29%)	2 / 11 (18.18%)	4 / 10 (40.00%)
occurrences (all)	2	4	7
White blood cell count decreased			
subjects affected / exposed	2 / 14 (14.29%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	2	5	2
Lymphocyte count decreased			

subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	0	2	2
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	1	4	3
Blood bilirubin increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
C-reactive protein increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Blood calcium increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood uric acid increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Contusion			
subjects affected / exposed	1 / 14 (7.14%)	3 / 11 (27.27%)	0 / 10 (0.00%)
occurrences (all)	1	4	0
Infusion related reaction			

subjects affected / exposed	4 / 14 (28.57%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	4	2	0
Rib fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Humerus fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cardiac failure congestive			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 14 (35.71%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	6	4	3
Coordination abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysaesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 14 (50.00%)	6 / 11 (54.55%)	6 / 10 (60.00%)
occurrences (all)	7	11	6
Thrombocytopenia			
subjects affected / exposed	2 / 14 (14.29%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	2	4	6
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	1	4
Haemolysis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Dry eye			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 14 (28.57%)	4 / 11 (36.36%)	3 / 10 (30.00%)
occurrences (all)	4	7	3
Nausea			
subjects affected / exposed	5 / 14 (35.71%)	3 / 11 (27.27%)	3 / 10 (30.00%)
occurrences (all)	5	3	4
Constipation			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Dental caries			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			

subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	2 / 14 (14.29%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Abdominal distension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gingival pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Mouth haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Dermal cyst			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Purpura			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Chronic kidney disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	2	2	2
Spinal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Bone pain			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Muscle spasms			

subjects affected / exposed	0 / 14 (0.00%)	3 / 11 (27.27%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Muscular weakness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Pathological fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	2	3	3
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	3 / 10 (30.00%)
occurrences (all)	1	0	3
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 14 (14.29%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	2	1	1

Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	3 / 11 (27.27%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Covid-19			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Enterocolitis infectious			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Hypomagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	1	1	3
Hypoalbuminaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	7	0
Hypophosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	7	0
Hyperuricaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2021	Amendment 1: • Address changes based on feedback from the Food and Drug Administration (FDA). • Target population was amended per FDA request. • Eligibility criteria was amended per FDA request. • The information related to dose limiting toxicity was amended per FDA request. • Study stopping rules based on a specified rate of unacceptable toxicity were added per FDA recommendation. • Inclusion criteria pertaining to previous lines of therapy for MM were amended per FDA request. • Exclusion criteria pertaining to dose of prednisone was amended per FDA request. • The information on route of administration of daratumumab was modified to provide clarity. • The information on dose modification and delays of magrolimab was modified to provide more clarity. • The information on bone marrow assessments was modified to provide more clarity. • The text on management of infusion related reactions was modified to provide more clarity. • New section on 'Management of Pneumonitis' was added per FDA request. • New section on 'Management of Other Non-hematologic Adverse Events' was added per FDA request. • The text on formulations of daratumumab was modified to provide more clarity. • The text toxicity management of pomalidomide was modified to provide more clarity. • The text for referring applicable product's label for bortezomib was added. • New references were added for 'Treatment-Related Toxicity monitoring'. • X added to line for Urine Immunofixation (UIFE), for consistency with Section 6.5.1 of the protocol. • The schedule of assessments (SOA) table was updated to specify peripheral smear separately. • Antidrug antibody sampling once in 12 weeks (Q12W) was removed from table.
05 May 2021	Amendment 2: • Changes to inclusion criteria #11: Updated to mitigate against a drop in hemoglobin with the initial dosing of magrolimab. Changes to inclusion criteria #22 and #25, and removal of inclusion criteria #21, #24, and #28: Updated based on feedback from external experts in the field of multiple myeloma in order to select appropriate patients for the study. Addition of inclusion criteria #21: Updated to ensure consistency with inclusion criteria for other combination arms. • Study Schema was updated to include 3 prior therapies, in line with Amendment 1. • Information related to time interval between completion of magrolimab infusion/injection and the initiation of daratumumab was removed. Daratumumab should be given before magrolimab with a 1 hour observation period in between. • Information on magrolimab discontinuation was amended per FDA request. • Corrected an error. Updated dosing duration in line with USPI for dosing days and cycle length for dose reductions.

12 October 2021	Amendment 3: • Text was added to allow use of approved generic or a biosimilar for combination agents. • New section was added to provide a description and summary of clinical data for carfilzomib. • The description of bortezomib was updated to remove redundant text that was added to a previous section. • Text was added to add a rationale for carfilzomib as the preferred proteasome inhibitor. • Study schema was updated to add carfilzomib as the preferred proteasome inhibitor. • The section 3.1.1. Safety Run-in Cohorts was updated to remove the need for additional safety follow-up evaluation based on the updated Cycle 3 dose for magrolimab. • Text updated to section 3.8.2. Pharmacokinetics/Biomarker Samples for Optional Future Research to include buccal samples. • Inclusion criteria was updated to indicate requirements for previous lines of therapy for patients. • Inclusion criteria were updated to add requirements for previous lines of therapy for patients who will receive magrolimab in combination with daratumumab. • Inclusion criteria were updated to add requirements for previous lines of therapy for patients who will receive magrolimab in combination with pomalidomide and dexamethasone. • Inclusion criteria were updated to add requirements for previous lines of therapy for patients who will receive magrolimab in combination with carfilzomib and dexamethasone. • Inclusion criteria were updated to add criteria for patients who will receive magrolimab in combination with bortezomib and dexamethasone. • Exclusion criteria was added to exclude patients who received any live vaccine within 4 weeks prior to treatment. • Text was updated to expand description of physical appearance of magrolimab. • New section was added to include a description of the formulation, packaging and labeling, and storage and handling of carfilzomib. • Text was updated to add a window for magrolimab dosing.
12 October 2021	Amendment 3: • New section was added to give instructions for dosage and administration of carfilzomib and dexamethasone. • Text was added to Magrolimab section to give guidance regarding dose delays and interruptions for the combination drugs. • Table 11 was updated to reflect new dosing regimen for magrolimab from Cycle 3 onwards. • Text was deleted to update guidance regarding dose delays and interruptions of daratumumab. • Text was updated to add recommendations for carfilzomib dose modifications and delays based on toxicity. • Text was added to clarify that live vaccines are prohibited before and during the study. • Table was updated to clarify prohibited prior medications for drug combinations with magrolimab. • Text added to clarify allowance of COVID-19 vaccines. • Text was revised to clarify type and screen procedures. • Text was updated to give instructions for toxicity management for carfilzomib. • The section was added to give instructions for toxicity management for carfilzomib. • The appendix was updated to include guidance for pregnancy and contraception for carfilzomib.

31 March 2022	Amendment 4: • Inclusion Criterion #10 (Section 4.2) was updated to indicate that hemoglobin level must be ≥ 9 g/dL prior to initial dose of study treatment. • Inclusion Criterion #11 (Section 4.2) was removed as there is no added clinical advantage of necessitating a hemoglobin threshold of 9.5 g/dL or more in patients with cardiac comorbidities. • Inclusion Criterion #20 (Section 4.2) was updated to remove the requirement for patients to have CD38-positive multiple myeloma. • Additional clarification on timing of magrolimab premedication was added to Section 5.3.1. • Type and Screen and Direct Antiglobulin Test (Section 6.2.2) was updated to remove details from this section and refer to Section 7.8.1.1. • Dosage and Administration of Magrolimab (Section 5.3.1) and Laboratory Assessments (Section 6.4.2) were updated to link to the hemoglobin monitoring and testing requirements detailed in Section 7.8.1.1. • Anemia management described in Anemia, Blood Cross-matching, and Packed Red Blood Cell Transfusion Procedures (Section 7.8.1.1) and its subsections was updated to clarify the risk of anemia in the first 2 weeks of treatment and provide additional guidance for enhanced anemia management. Updates include adding the requirement to confirm hemoglobin level prior to magrolimab dosing and within 24 hours after the first 2 doses of magrolimab. • Thromboembolic Events (Section 7.8.1.3) text was added to match the investigator's brochure (IB) Edition 9. • Hemagglutination and Microangiopathy text was deleted from Section 7.8.1.3 Toxicity Management to match the IB Edition 9. • Text was updated to align the publications language in the clinical trial agreement (Section 9.2.2).
31 March 2022	Amendment 4: • Appendix 10 was added to include the Myeloma Frailty Score Calculator Additional change(s) to the protocol include the following: • Administrative, editorial, and formatting updates, changes, corrections, and clarifications were made throughout, where appropriate, including section numbering and references. • Changes in the body of the protocol were also updated in the synopsis and study procedures tables, as appropriate.
31 May 2022	Amendment 5: • Lowered the stopping boundary due to toxicity from greater than 33% to greater than 25% of patients experiencing a Grade 4 or higher treatment related AE (Section 3.1.3; Table 3) in order to increase patient safety during the dose expansion phase of the study. • Clarified the process for analyzing bone marrow samples during screening. (Section 6.2). • Clarified the processes for investigator evaluation of disease response assessments by providing additional detail regarding which assessments would be analyzed at the central laboratory versus locally (Section 6.5.2 and 6.5.4).

02 November 2023	Amendment 6: • Removal of posttreatment follow-up for disease progression and survival follow-up assessments and secondary endpoints for progression-free survival (PFS) and overall (OS) as efficacy data will no longer be collected after the end-of-treatment (EOT) visit. • Removal of exploratory endpoint for minimal residual disease (MRD) negativity rate as central laboratory assessment of MRD is no longer required. • Removal of exploratory endpoints/analyses to evaluate the association of each biomarker or combination of biomarkers with clinical outcomes as there are no plans to perform these analyses anymore. • Guidance for the use of corticosteroids as premedication for the first few infusions of magrolimab has been incorporated to align with the information in Edition 12 of the Investigator's Brochure. • Clarification of standard of care procedure language incorporated from Administrative Amendment 1 for Protocol Amendment 5. • Removal of receptor occupancy assessment. • Removal of the requirement for multiple myeloma, tumor response, and bone marrow assessments to be performed by a central laboratory. These assessments may now be performed by a central or local laboratory based on investigator preference. • Removal of FACT-MM questionnaire assessment as patient-reported outcome data are no longer required. • Guidance for the management of infusion-related reactions has been updated to incorporate the use of corticosteroids as premedication during the first few infusions of magrolimab, and to incorporate guidance for discontinuation of magrolimab in certain cases. This was done to align with the information in Edition 12 of the Investigator's Brochure. • Toxicity management section for magrolimab has been updated to include guidelines for dose delay and discontinuation in case of severe neutropenia and serious infections to align with the information in Edition 12 of the Investigator's Brochure.
02 November 2023	Amendment 6: • Clarification that assessment of quantitative Ig levels is to be performed for patients with IgA and IgD myelomas to align with Section 6.5.1. • Contraception appendix has been updated to reflect the latest nonclinical embryo-fetal development toxicity data. • Global Patient Safety (GLPS) has been updated to Patient Safety (PS) to reflect the new department name.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 April 2024	The study was terminated early due to the Sponsor's decision to discontinue development of the investigational drug and program closure.	-

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36779512