Clinical trial results:
An Open-label, Phase 2 Study Treating Subjects with First or Second Relapse of Multiple Myeloma with Carfilzomib, Pomalidomide, and Dexamethasone (KPd)

Summary

EudraCT number	2019-001169-34
Trial protocol	DK FR GR ES DE IT
Global end of trial date	01 October 2024

Results information

Result version number	v1 (current)
This version publication date	11 September 2025
First version publication date	11 September 2025

Trial information

Trial identification

Sponsor protocol code	20180117

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04191616
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	01 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to estimate the overall response rate.

Protection of trial subjects:

The study protocol and all amendments, the informed consent form, and any accompanying materials provided to the participants were reviewed and approved by an Institutional Review Board (IRB) or Independent Ethics Committee (IEC) at each study center. This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. The investigator or his/her designee informed the participant of all aspects pertaining to the participant's participation in the study before any screening procedures were performed.

Background therapy:

Participants may receive intravenous (IV) pre-hydration (normal saline or other appropriate IV fluid) prior to each carfilzomib infusion during cycle 1. Investigators must consider IV pre-hydration in participants at high-risk for tumor lysis or renal toxicity.

Evidence for comparator: -

Actual start date of recruitment	06 August 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 24
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	54
EEA total number of subjects	48

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)	23
From 65 to 84 years	30
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 25 study centers in Denmark, France, Germany, Greece, Italy, Spain, and the United States from 06 August 2020 to 01 October 2024.

Pre-assignment

Screening details:

Participants with relapsed multiple myeloma whose disease was refractory to lenalidomide were enrolled.

Pre-assignment period milestones

Number of subjects started	54
Number of subjects completed	52

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not receive study treatment: 2

Period 1

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

Arms

Arm title	Carfilzomib with Pomalidomide and Dexamethasone (KPd)

Arm description:

Carfilzomib was administered intravenously on days 1, 8, and 15 (± 2 days) of each 28-day cycle for up to 12 cycles or progression or end of study. A dose of 20 mg/m^2 was administered on day 1 of cycle 1; all subsequent doses were 56 mg/m^2. From cycle 13, the frequency of carfilzomib administration was reduced to days 1 and 15 (± 2 days) per cycle until progression or end of study. Dexamethasone was administered orally or intravenously at a dose of 40 mg on days 1, 8, 15, and 22 of each cycle during cycles 1 to 12, and at a dose of 20 mg on days 1 and 15 from cycle 13 until progression or end of study. Pomalidomide 4 mg was administered orally on days 1 to 21 of each cycle until progression or end of study.

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:

Carfilzomib was administered intravenously on days 1, 8, and 15 (± 2 days) of each 28-day cycle for up to 12 cycles or progression or end of study. A dose of 20 mg/m^2 was administered on day 1 of cycle 1; all subsequent doses were 56 mg/m^2. From cycle 13, the frequency of carfilzomib administration was reduced to days 1 and 15 (± 2 days) per cycle until progression or end of study.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Solution for infusion, Solution for injection
Routes of administration	Oral use, Intramuscular and intravenous use

Dosage and administration details:

Dexamethasone was administered orally or intravenously at a dose of 40 mg on days 1, 8, 15, and 22 of

each cycle during cycles 1 to 12, and at a dose of 20 mg on days 1 and 15 from cycle 13 until progression or end of study.

Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pomalidomide 4 mg was administered orally on days 1 to 21 of each cycle until progression or end of study.

Number of subjects in period 1[1]	Carfilzomib with Pomalidomide and Dexamethasone (KPd)
Started	52
Completed	0
Not completed	52
Consent withdrawn by subject	4
Death	37
Sponsor decision	11

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: The number of participants in the baseline period is equal to the number of participants who received study treatment.

Baseline characteristics

Reporting groups

Reporting group title	Carfilzomib with Pomalidomide and Dexamethasone (KPd)

Reporting group description:

Carfilzomib was administered intravenously on days 1, 8, and 15 (± 2 days) of each 28-day cycle for up to 12 cycles or progression or end of study. A dose of 20 mg/m^2 was administered on day 1 of cycle 1; all subsequent doses were 56 mg/m^2. From cycle 13, the frequency of carfilzomib administration was reduced to days 1 and 15 (± 2 days) per cycle until progression or end of study. Dexamethasone was administered orally or intravenously at a dose of 40 mg on days 1, 8, 15, and 22 of each cycle during cycles 1 to 12, and at a dose of 20 mg on days 1 and 15 from cycle 13 until progression or end of study. Pomalidomide 4 mg was administered orally on days 1 to 21 of each cycle until progression or end of study.

Reporting group values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)	Total	
Number of subjects	52	52	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	23	23	
From 65-84 years	28	28	
85 years and over	1	1	
Gender Categorical Units: Subjects			
Female	28	28	
Male	24	24	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	4	
Not Hispanic or Latino	45	45	
Unknown or Not Reported	3	3	
Race/Ethnicity Units: Subjects			
Asian	1	1	
Black or African American	1	1	
White	47	47	
Other	3	3	

End points

End points reporting groups

Reporting group title	Carfilzomib with Pomalidomide and Dexamethasone (KPd)

Reporting group description:

Carfilzomib was administered intravenously on days 1, 8, and 15 (± 2 days) of each 28-day cycle for up to 12 cycles or progression or end of study. A dose of 20 mg/m^2 was administered on day 1 of cycle 1; all subsequent doses were 56 mg/m^2. From cycle 13, the frequency of carfilzomib administration was reduced to days 1 and 15 (± 2 days) per cycle until progression or end of study. Dexamethasone was administered orally or intravenously at a dose of 40 mg on days 1, 8, 15, and 22 of each cycle during cycles 1 to 12, and at a dose of 20 mg on days 1 and 15 from cycle 13 until progression or end of study. Pomalidomide 4 mg was administered orally on days 1 to 21 of each cycle until progression or end of study.

Primary: Overall Response Rate (ORR) as Assessed by the Independent Review Committee (IRC)

End point title	Overall Response Rate (ORR) as Assessed by the Independent Review Committee (IRC)[1]

End point description:

Overall response was defined as the best overall confirmed response of: Complete response (CR): Negative immunofixation on serum and urine, soft tissue plasmacytomas disappearance, < 5% plasma cells in bone marrow (BM). Stringent CR (sCR): CR and normal serum free light chain ratio and no clonal cells in BM. Very Good Partial Response (VGPR): Serum and urine M-protein detectable by immunofixation or ≥ 90% reduction in serum M-protein (urine M-protein level < 100 mg/24-h). PR: ≥ 50% reduction of serum M-protein and 24-h urinary M-protein by ≥ 90% or to < 200 mg/24-h. Assessment was by IRC per International Myeloma Working Group Uniform Response Criteria (IMWG-URC). The 90% confidence intervals were estimated using the Clopper-Pearson method (1994).

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Primary

End point timeframe:

From day 1 cycle 1 until the primary analysis (PA) data cutoff (DCO); the mean duration of KPd treatment as of the DCO was 42.0 weeks

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: Formal comparative statistical analysis was not pre-specified for this outcome measure.

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of participants				
number (confidence interval 90%)	57.7 (45.4 to 69.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point description:

TEAEs were defined as events with onset on or after the administration of the first dose of any study treatment and within the end of study, or 30 days after the last dose of any study treatment, whichever one was earlier, excluding events reported after end of study date.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

From the first dose of any study treatment until the end of study or 30 days after the last dose of any study treatment, whichever occured earlier; Median (min, max) was 8.5 (1.0, 46.6) months

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants	50			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Minimal Residual Disease Negative Complete Response (MRD[-]CR) as Assessed by the IRC

End point title	Percentage of Participants with a Minimal Residual Disease Negative Complete Response (MRD[-]CR) as Assessed by the IRC

End point description:

The MRD[-]CR rate was defined as the percentage of participants who reached MRD[-]CR at the 12 month landmark (8- to 13-month window). MRD[-]CR was defined as the achievement of CR (including sCR or better) per IMWG-URC by IRC assessment and MRD[-] status at a sensitivity of 10^-5 using next-generation sequencing based method in the bone marrow. The 90% CIs were estimated using the Clopper-Pearson method (1994).

The safety analysis set included all participants who received at least 1 dose of carfilzomib. The analysis was pre-specified until PA DCO only.

End point type	Secondary

End point timeframe:

Day 1 cycle 1 to month 12 (8 to 13 month window)

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of participants				
number (confidence interval 90%)	3.8 (0.7 to 11.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression Free Survival (PFS) as Assessed by the IRC

End point title	Kaplan-Meier Estimate of Progression Free Survival (PFS) as Assessed by the IRC

End point description:

PFS was defined as time from start of treatment until progression or death from any cause. Medians and percentiles were estimated using the Kaplan-Meier method by Klein and Moeschberger (1997). 90% CIs for medians were estimated using the method by Klein and Moeschberger (1997) with log-log transformation.

9999 = Result was not estimable.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the PA DCO; the mean duration of KPd treatment as of the DCO was 42.0 weeks

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: months				
median (confidence interval 90%)	11.1 (6.5 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Response as Assessed by the IRC

End point title	Kaplan-Meier Estimate of Duration of Response as Assessed by the IRC

End point description:

Disease response and progression were determined using IMWG-URC. Durations were calculated for responders. Medians and percentiles were estimated using the Kaplan-Meier method. 90% CIs for medians and percentiles were estimated using the method by Klein and Moeschberger (1997) with log-log transformation.

9999 = Result was not estimable.

The safety analysis set included all participants who received at least 1 dose of carfilzomib. Only participants who achieved a partial response or better were included in the analysis.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the PA DCO; the mean duration of KPd treatment as of the DCO was 42.0 weeks

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: months				
median (confidence interval 90%)	20.3 (9.2 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response as Assessed by the IRC

End point title	Time to Response as Assessed by the IRC

End point description:

Durations were calculated for responders. Time to response was defined as the time from start of any study treatment date to the earliest date when confirmed sCR, CR, VGPR, or partial response (PR) was first achieved.

The safety analysis set included all participants who received at least 1 dose of carfilzomib. Only participants who achieved a partial response or better were included in the analysis.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the PA DCO; the mean duration of KPd treatment as of the DCO was 42.0 weeks

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: months				
median (full range (min-max))	1.0 (1 to 2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Overall Survival (OS)

End point title	Kaplan-Meier Estimate of Overall Survival (OS)

End point description:

OS was defined as the time from the start of treatment until death from any cause. Medians and percentiles were estimated using the Kaplan-Meier method. 90% CIs for medians were estimated using the method by Klein and Moeschberger (1997) with log-log transformation.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the EOS; the mean duration of KPd treatment was 55.3 weeks.

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: months				
median (confidence interval 90%)	17.6 (11.2 to 23.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving MRD[-] Response

End point title	Number of Participants Achieving MRD[-] Response

End point description:

MRD[-] response was defined as achievement of MRD[-] status using next generation sequencing (NGS) based method in the bone marrow at any time.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the end of study (EOS); the mean duration of KPd treatment as of the EOS was 55.3 weeks

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Sustained MRD[-]CR for at Least 12 Months as Assessed by the IRC

End point title	Number of Participants with Sustained MRD[-]CR for at Least 12 Months as Assessed by the IRC

End point description:

MRD[-]CR at the 12 months landmark was defined as achievement of CR (including sCR or better) per IMWG-URC by IRC and MRD[-] status at a sensitivity of 10^-5 using NGS based method in the bone marrow at the 12 months landmark (from 8 months to 13 months window). Maintaining MRD[-]CR for at least 12 months (- 4 weeks) was considered as sustained.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

Day 1 cycle 1 to month 12 (8 to 13 month window)

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Sustained MRD[-]CR at Month 24 as Assessed by the IRC

End point title	Number of Participants with Sustained MRD[-]CR at Month 24 as Assessed by the IRC

End point description:

Sustained MRD[-]CR at 24 months included participants that maintained MRD[-]CR for 12 months or more after achieving MRD[-]CR status at 12 months.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

Day 1 cycle 1 to month 26 (19 to 26 month window)

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Best Overall Confirmed Response of CR or Better as Assessed by the IRC

End point title	Number of Participants with Best Overall Confirmed Response of CR or Better as Assessed by the IRC

End point description:

The number of safety analysis set participants whose best overall response was sCR or CR per IMWG-URC over the duration of the study.

The safety analysis set included all participants who received at least 1 dose of carfilzomib.

End point type	Secondary

End point timeframe:

From day 1 cycle 1 until the PA DCO; the mean duration of KPd treatment as of the DCO was 42.0 weeks

End point values	Carfilzomib with Pomalidomide and Dexamethasone (KPd)			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: participants	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Death: 1st study drug to EOS, also after EOS; Median (min, max) was 16.5 (1.0, 47.0) months. Adverse events: 1st dose of any study treatment to earliest of EOS or 30 days after last dose of any study treatment; Median (min, max) was 8.5 (1.0, 46.6) months

Adverse event reporting additional description:

All-cause mortality is reported for all participants enrolled in the study. Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Carfilzomib with Pomalidomide and Dexamethasone (KPd)

Reporting group description:

Carfilzomib was administered intravenously on days 1, 8, and 15 (± 2 days) of each 28-day cycle for up to 12 cycles or progression or end of study. A dose of 20 mg/m^2 was administered on day 1 of cycle 1; all subsequent doses were 56 mg/m^2. From cycle 13, the frequency of carfilzomib administration was reduced to days 1 and 15 (± 2 days) per cycle until progression or end of study. Dexamethasone was administered orally or intravenously at a dose of 40 mg on days 1, 8, 15, and 22 of each cycle during cycles 1 to 12, and at a dose of 20 mg on days 1 and 15 from cycle 13 until progression or end of study. Pomalidomide 4 mg was administered orally on days 1 to 21 of each cycle until progression or end of study.

Serious adverse events	Carfilzomib with Pomalidomide and Dexamethasone (KPd)		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 52 (42.31%)		
number of deaths (all causes)	37		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Left ventricular failure			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteitis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bone pain			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Carfilzomib with Pomalidomide and Dexamethasone (KPd)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 52 (92.31%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	10		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	10		
Oedema peripheral			
subjects affected / exposed	11 / 52 (21.15%)		
occurrences (all)	12		
Fatigue			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	16		
Asthenia			

subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	20		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Dyspnoea			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	10		
Cough			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	7		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	6		
Investigations			
Platelet count decreased			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	5		
Nervous system disorders			
Syncope			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Paraesthesia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Thrombocytopenia			
subjects affected / exposed	16 / 52 (30.77%)		
occurrences (all)	30		
Neutropenia			

subjects affected / exposed	17 / 52 (32.69%)		
occurrences (all)	42		
Anaemia			
subjects affected / exposed	16 / 52 (30.77%)		
occurrences (all)	21		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	8		
Nausea			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	11		
Diarrhoea			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	10		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	7		
Muscle spasms			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	8		
Bone pain			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	6		

Back pain			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
Respiratory tract infection			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Lower respiratory tract infection			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	5		
COVID-19			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	9		
Upper respiratory tract infection			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	7		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2019	• Cohort 1: Carfilzomib, Daratumumab, and Dexamethasone was removed. • Hepatic Insufficiency for pomalidomide was added. • Secondary endpoint of frequency of sustained MRD response was added. • Statistical analysis section was updated to include 12 month landmark. • Objectives and endpoints were clarified. • NGS-based method for evaluating MRD was added. • Title of protocol was updated to include second relapse. • IRC was added. • Number of subjects and number of sites were updated. • Study rationale and benefit/risk sections were updated with updated data. • Bone targeting agents were added to recommended therapies.
13 May 2020	• Prophylaxis for Hepatitis B virus reactivation to other protocol-required therapies was added. • Hepatitis B dose modification was added. • MRD assessments were changed from a ± 2-week window, to a ± 4-week window. • The primary objective was updated from estimating the efficacy by rate of MRD[-] response of KPd to estimating the rate of MRD[-]CR. • Screening was updated regarding fetal toxicity, beginning 4 weeks prior to initiating treatment with pomalidomide. • Clarifications were made to PFS, OS, and CR in efficacy analyses. • Dose modification in abnormalities from tumor lysis syndrome were added. • Windows for radiological plasmacytoma assessments were extended from every 12 weeks to every 12 weeks ± 2 weeks. • Screening evaluations for disease specific assessments, measurable disease, rescreening, echocardiograms, pulmonary function tests, bone lesions, and plasmacytomas were changed from 30 to 28 days. • 2 contraceptive methods were removed to align with the Summary of Product Characteristics for pomalidomide: (1) intrauterine devices and (2) combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation. • Reporting requirement for start and stop time of Pomalidomide administration was removed.
26 March 2021	• The requirement of daratumumab exposure was removed. • The ORR was updated as a key secondary endpoint to further designate this endpoint as clinically important and pre-specify the order for analysis. • The number of sites were updated from 35 to 45. • The carfilzomib dose modification guidelines for nonhematologic toxicities were updated. • The statistical considerations were updated, given newly available data that includes outcomes of subjects who are refractory to lenalidomide. • The safety reporting and birth control requirements were updated per the current protocol template.
16 May 2022	• Primary endpoint was changed to ORR, and MRD[-] CR rate was moved to secondary endpoint. • The hypothesis and statistical consideration sections were updated to align with updated endpoints. • Pomalidomide modification guidelines were updated for nonhematologic toxicities. • Statements on discontinuation of recruitment after 54 subjects enrolled were added; decision was made because of challenges to enrollment in part due to evolving changes in multiple myeloma treatment landscape.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported