Clinical trial results:
A Phase 2, Randomized, Open-Label Study Comparing Oral Ixazomib/Dexamethasone and Oral Pomalidomide/Dexamethasone in Relapsed and/or Refractory Multiple Myeloma

Summary

EudraCT number	2016-004742-28
Trial protocol	CZ SE GB DE DK NL BE ES GR IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	19 August 2021
First version publication date	19 August 2021

Trial information

Trial identification

Sponsor protocol code	C16029

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03170882
WHO universal trial number (UTN)	U1111-1188-2677

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, MA, United States, 02421
Public contact	Study Director, Takeda, +1 8778253327, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, +1 8778253327, TrialDisclosures@takeda.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	Interim
Date of interim/final analysis	01 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2020
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study was to learn if ixazomib, given with dexamethasone, stops the cancer from getting worse in people with relapsed or refractory multiple myeloma. It was compared to another medicine called pomalidomide, given with dexamethasone with people with the same condition.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Norway: 15
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Turkey: 7
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Australia: 10
Worldwide total number of subjects	122
EEA total number of subjects	68

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)	31
From 65 to 84 years	88
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 54 investigative sites in Australia, Turkey, Czech Republic, France, Germany, Italy, Netherlands, Norway, Spain, Israel, United Kingdom, Sweden, Greece, and Russian Federation from 01 August 2017 up to 01 August 2020. This study is ongoing.

Pre-assignment

Screening details:

Participants with a diagnosis of relapsed and/or refractory multiple myeloma (RRMM) who received at least 2 prior lines of therapy were enrolled in 2:3 ratio to receive pomalidomide + dexamethasone or ixazomib + dexamethasone in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pomalidomide 4 mg + Dexamethasone 40 mg

Arm description:

Pomalidomide 4 mg, capsules, orally, once daily on Days 1 to 21 of each 28-day cycle, plus dexamethasone 40 mg, (or 20 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 8, 15, and 22 of each 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Arm type	Active comparator
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pomalidomide capsules

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

Dosage and administration details:

Dexamethasone tablets

Arm title	Ixazomib 4 mg + Dexamethasone 20 mg

Arm description:

Ixazomib 4 mg as starting dose, capsules, orally, once daily on Days 1, 8, and 15 of each 28-day cycle, with escalation to 5.5 mg at the start of Cycle 2 for participants who tolerated the 4 mg dose in Cycle 1, plus dexamethasone 20 mg (or 10 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 2, 8, 9, 15, 16, 22, and 23 of every 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Arm type	Experimental

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

Dosage and administration details:

Dexamethasone tablets

Investigational medicinal product name	Ixazomib
Investigational medicinal product code	
Other name	NINLARO MLN9708
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ixazomib capsules

Number of subjects in period 1	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg
Started	49	73
Treated: Safety Population	47	72
ITT PRO Population	45	70
Completed	20	22
Not completed	29	51
Consent withdrawn by subject	4	6
Death	15	29
Ongoing	10	14
Lost to follow-up	-	1
Reason not Specified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Pomalidomide 4 mg + Dexamethasone 40 mg
Reporting group description:	
Pomalidomide 4 mg, capsules, orally, once daily on Days 1 to 21 of each 28-day cycle, plus dexamethasone 40 mg, (or 20 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 8, 15, and 22 of each 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.	
Reporting group title	Ixazomib 4 mg + Dexamethasone 20 mg
Reporting group description:	
Ixazomib 4 mg as starting dose, capsules, orally, once daily on Days 1, 8, and 15 of each 28-day cycle, with escalation to 5.5 mg at the start of Cycle 2 for participants who tolerated the 4 mg dose in Cycle 1, plus dexamethasone 20 mg (or 10 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 2, 8, 9, 15, 16, 22, and 23 of every 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.	

Reporting group values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg	Total
Number of subjects	49	73	122
Age categorical Units: Subjects			
Adults (18-64 years)	13	18	31
From 65-84 years	36	52	88
85 years and over	0	3	3
Age Continuous Units: years			
arithmetic mean	67.7	70.6	
standard deviation	± 8.33	± 8.60	-
Sex: Female, Male Units: participants			
Female	23	38	61
Male	26	35	61
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	3	5
Not Hispanic or Latino	42	65	107
Unknown or Not Reported	5	5	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	46	69	115
More than one race	0	0	0
Unknown or Not Reported	3	2	5
Region of Enrollment Units: Subjects			
Russia	8	15	23

Norway	7	8	15
Italy	9	5	14
France	3	9	12
United Kingdom	3	6	9
Germany	1	6	7
Turkey	4	3	7
Spain	2	4	6
Israel	3	2	5
Czech Republic	1	3	4
Netherlands	2	2	4
Greece	0	3	3
Sweden	2	1	3
Australia	4	6	10
Baseline Height			
Units: cm			
arithmetic mean	166.59	165.01	
standard deviation	± 8.740	± 10.475	-
Baseline Weight			
Units: kg			
arithmetic mean	75.75	74.36	
standard deviation	± 16.160	± 17.426	-
Baseline Body Surface Area			
Units: m^2			
arithmetic mean	1.864	1.837	
standard deviation	± 0.2203	± 0.2430	-

End points

End points reporting groups

Reporting group title	Pomalidomide 4 mg + Dexamethasone 40 mg

Reporting group description:

Pomalidomide 4 mg, capsules, orally, once daily on Days 1 to 21 of each 28-day cycle, plus dexamethasone 40 mg, (or 20 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 8, 15, and 22 of each 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Reporting group title	Ixazomib 4 mg + Dexamethasone 20 mg

Reporting group description:

Ixazomib 4 mg as starting dose, capsules, orally, once daily on Days 1, 8, and 15 of each 28-day cycle, with escalation to 5.5 mg at the start of Cycle 2 for participants who tolerated the 4 mg dose in Cycle 1, plus dexamethasone 20 mg (or 10 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 2, 8, 9, 15, 16, 22, and 23 of every 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS:Time from randomisation to first occurrence of confirmed progressive disease(PD) assessed by investigator by International Myeloma Working Group(IMWG) response criteria/death, whichever comes first.PD:Increase of >=25% from nadir in:Serum M component(increase>=0.5g/dl);Urine M-component (increase>=200 mg/24hr);In participants without measurable serum and urine M-protein levels difference between involved and uninvolved free light chain(FLC) increase >10mg/dl;In participants without measurable serum and urine M protein levels, without measurable disease by FLC level:bone marrow plasma cell percentage >=10%;Development of new/increase in size of existing bone lesions/soft tissue plasmacytomas;development of hypercalcemia (>11.5mg/dL corrected serum calcium) attributed solely to plasma cell proliferative disease.ITT Population:all participants randomised. Participants without documentation of PD were censored at date of last response assessment that is stable disease(SD) or better.

End point type	Primary

End point timeframe:

From date of randomisation until first occurrence of confirmed disease progression or death due to any cause, whichever occurs first (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: months				
median (confidence interval 95%)	4.8 (3.745 to 8.542)	7.1 (3.943 to 11.138)		

Statistical analyses

Statistical analysis title	Statistical Analysis for PFS
Comparison groups	Pomalidomide 4 mg + Dexamethasone 40 mg v Ixazomib 4 mg + Dexamethasone 20 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.477
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.847
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.535
upper limit	1.341

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from randomisation to death from any cause, up to 3 years are reported. ITT Population included all participants who were randomised. Participants without documented death at the time of analysis were censored at the date last known to be alive. 99999 indicates that median and 95% CI was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From date of randomisation to death due to any cause (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: months				
median (confidence interval 95%)	99999 (13.963 to 99999)	18.8 (10.973 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis for OS
Comparison groups	Pomalidomide 4 mg + Dexamethasone 40 mg v Ixazomib 4 mg + Dexamethasone 20 mg

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.265
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.427
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.761
upper limit	2.677

Notes:

[1] - HR obtained by unadjusted Cox's proportional hazard regression model stratified by age, ISS and prior lines of therapy. HR <1 was deemed to indicate longer survival time in Ixazomib + Dexamethasone arm as compared to Pomalidomide + Dexamethasone arm.

Secondary: Percentage of Participants with Overall Response

End point title	Percentage of Participants with Overall Response

End point description:

Overall Response Rate(ORR) was defined as the percentage of participants who achieved partial response(PR), very good partial response(VGPR), or complete response(CR) based on laboratory results and IRC assessment using modified IMWG criteria. PR: >=50% reduction of serum M protein+reduction in 24-hour urinary M protein by>=90% or to <200 mg/24-hour; if M protein is not measurable,>=50% decrease in difference between involved and uninvolved FLC levels is required; if not measurable by FLC,>=50% reduction in bone marrow plasma cells, when baseline value>=30% and; if present at baseline,>=50% reduction in size of soft tissue plasmacytomas is required. VGPR: serum and urine M-protein detectable by immunofixation but not on electrophoresis or>=90% reduction in serum M-protein+urine M-protein level<100 mg/24-hour. CR: negative immunofixation on serum+urine; disappearance of soft tissue plasmacytomas;<5% plasma cells in bone marrow. ITT Population: all participants who were randomised.

End point type	Secondary

End point timeframe:

From date of randomisation until first documentation of CR, VGPR or PR (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: percentage of participants				
number (confidence interval 95%)	41 (27 to 56)	38 (27 to 50)		

Statistical analyses

Statistical analysis title	Statistical Analysis for ORR
Comparison groups	Pomalidomide 4 mg + Dexamethasone 40 mg v Ixazomib 4 mg + Dexamethasone 20 mg

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.634
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.9

Notes:

[2] - OR was based on logistic regression model with treatment group as categorical predictor variable and age, ISS and prior lines of therapy. OR >1 was deemed to indicate better response in Ixazomib+Dexamethasone arm over Pomalidomide+Dexamethasone arm.

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR:Time from first documentation of CR/PR/VGPR to first documentation of PD.IMWG criteria, PR:>=50%lower of serumMprotein+reduced 24hr urinary Mprotein >=90% to <200 mg/24-hour or >=50%decreaseed difference between involved-uninvolved FLC level/>=50%lower bone marrow (BM) plasmacell,if >=30%at Baseline/>=50%lower size of softtissue plasmacytomas. VGPR: serum+urineprotein detected by immunofixation (IM)/>=90% reduced serum Mprotein+urine Mprotein level <100mg/24hr. CR:negative IM on serum&urine+disappeared soft tissue plasmacytomas+<5%plasmacell in BM. PD:serumMcomponent >=0.5g/dl/urineMcomponent >=200 mg/24hr/ difference between involved-uninvolved FLC level increase >10 mg/dl/BM plasma cell >=10%/developed new/increased size of existing bone lesion/soft tissue plasmacytoma/hypercalcemia. Response Evaluable Population:participants with confirmed PR,or PR/VGPR/CR.Responders were reported.99999=upper limit of 95%CI not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From date of first documentation of CR, VGPR or PR until first occurrence of confirmed disease progression or death due to any cause, whichever occurs first (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	28		
Units: months				
median (confidence interval 95%)	14.3 (3.713 to 99999)	14.8 (10.152 to 19.614)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

Time to response was defined as the time from randomisation to the first documentation of PR/VGPR/CR. Per IMWG criteria, PR: >=50% reduction of serum M protein + reduction in 24-hour urinary M protein by >=90% or to <200 mg/24-hour; if M-protein is not measurable, >=50% decrease in difference between involved and uninvolved FLC levels is required; if not measurable by FLC, >=50% reduction in bone marrow plasma cells, when Baseline value >=30% and; if present at Baseline, >=50% reduction in size of soft tissue plasmacytomas is required. VGPR: serum and urine M-protein detectable by immunofixation but not on electrophoresis or >=90% reduction in serum M-protein + urine M-protein level <100 mg/24-hour. CR: negative immunofixation on serum + urine; disappearance of soft tissue plasmacytomas; <5% plasma cells in bone marrow. Response Evaluable Population included all participants with multiple myeloma who had documentation of a confirmed PR, or PR/VGPR/CR.

End point type	Secondary

End point timeframe:

From date of randomisation until first documentation of CR, VGPR or PR (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: months				
median (confidence interval 95%)	1.1 (0.953 to 2.037)	2.0 (1.906 to 2.858)		

Statistical analyses

Statistical analysis title	Statistical Analysis for TOR
Comparison groups	Pomalidomide 4 mg + Dexamethasone 40 mg v Ixazomib 4 mg + Dexamethasone 20 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.288
upper limit	1.073

Notes:

[3] - HR was obtained by unadjusted Cox's proportional hazard regression model stratified by age, ISS, prior lines of therapy. HR >1 was deemed to indicate quicker response time in Ixazomib + Dexamethasone arm over Pomalidomide + Dexamethasone arm.

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)

End point description:

TTP was defined as the time from the date of randomisation to first documentation of PD. Per IMWG criteria, PD required 1 of the following: Increase of >=25% from nadir in: Serum M-component

(increase must be >=0.5 g/dl; Urine M-component (increase must be >=200 mg/24-hour); In participants without measurable serum and urine M-protein levels difference between involved and uninvolved FLC levels increase of >10 mg/dl; In participants without measurable serum and urine M protein levels and without measurable disease by FLC level: Bone marrow plasma cell percentage must be >=10%; Development of new or increase in size of existing bone lesions or soft tissue plasmacytomas; Development of hypercalcemia (>11.5 mg/dL corrected serum calcium) attributed solely to plasma cell proliferative disease. ITT Population: all participants who were randomised. Participants without documentation of PD at the time of analysis are censored at the date of last response assessment that is SD or better.

End point type	Secondary

End point timeframe:

From date of randomisation until first occurrence of confirmed disease progression or death due to any cause, whichever occurs first (Up to approximately 3 years)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: months				
median (confidence interval 95%)	5.1 (3.844 to 12.485)	8.4 (5.684 to 13.306)		

Statistical analyses

Statistical analysis title	Statistical Analysis for TTP
Comparison groups	Pomalidomide 4 mg + Dexamethasone 40 mg v Ixazomib 4 mg + Dexamethasone 20 mg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.459
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.506
upper limit	1.361

Notes:

[4] - HR: obtained by unadjusted Cox's proportional hazard regression model stratified by age,ISS,prior lines of therapy. HR<1 was deemed to indicate better disease progression prevention in Ixazomib+Dexamethasone arm over Pomalidomide+Dexamethasone arm.

Secondary: Health-Related Quality of Life (HRQOL) Based on European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire- Core 30 (EORTC QLQ-C30) Physical Domain Score

End point title	Health-Related Quality of Life (HRQOL) Based on European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire- Core 30 (EORTC QLQ-C30) Physical Domain Score

End point description:

The EORTC QLQ-C30 contains 30 items across 5 functional scales (physical, role, cognitive, emotional, and social), 9 symptom scales (fatigue, nausea and vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, and financial difficulties) and a global health status/quality of life (QOL) scale. The physical domain consisted of 5 items covering participant's daily physical activities on a scale from 1 (not at all) to 4 (very much). Raw scores were linearly transformed to a total score between 0-100, with a high score indicating better physical functioning. ITT PRO Population included participants with a measurement at study entry and at least one post study entry measurement for at least 1 subscale on all 3 questionnaires (EORTC QLQ-C30, EORTC Multiple Myeloma Module 20 [QLQ-MY20] and EuroQol 5-Dimensional Health Questionnaire [EQ-5D-5L]). 'n' indicates number analysed are the number of participants with data available for analyses at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (EOT) (Up to 28 cycles, each cycle was of 28 days)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	70		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 45, 70)	67.0 (± 21.97)	67.9 (± 22.08)		
End of Treatment (n= 28, 42)	52.4 (± 28.03)	56.5 (± 26.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQOL Based on EORTC QLQ-C30 Functional Scale Score

End point title	HRQOL Based on EORTC QLQ-C30 Functional Scale Score

End point description:

The EORTC QLQ-C30 contains 30 items across 5 functional scales (FS)-physical,role,cognitive,emotional, & social, 9 symptom scales(SS)- fatigue,nausea and vomiting,pain,dyspnea,sleep disturbance,appetite loss,constipation,diarrhea, & financial difficulties and a QOL scale.Most of the 30 items had 4 response levels(not at all,a little,quite a bit,and very much), with 2 questions relying on a 7-point numeric rating scale.Raw scores were linearly transformed to a total functional scale score between 0 to 100.For the functional scales and the global health status/QOL scale, higher scores represent better QOL;for the symptom scales, lower scores represent better QOL.ITT PRO Population:participants with a measurement at study entry and at least one post study entry measurement for at least 1 subscale on all 3 questionnaires(EORTC QLQ-C30,EORTC QLQ-MY20 & EQ-5D-5L).'n' indicates number analysed are the number of participants with data available for analyses at

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 28 cycles, each cycle was of 28 days)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	70		
Units: score on a scale				
arithmetic mean (standard deviation)				
Global Health Status/QoL:Baseline(n=45,70)	57.0 (± 20.72)	60.8 (± 21.16)		
Global Health Status/QoL:EOT(n=27,42)	47.8 (± 19.56)	48.2 (± 19.61)		
Role(FS):Baseline(n=45,70)	67.4 (± 28.42)	67.9 (± 29.67)		
Role(FS):EOT(n=28,42)	47.6 (± 27.86)	49.2 (± 27.04)		
Emotional (FS):Baseline(n=45,70)	74.9 (± 21.19)	83.1 (± 21.70)		
Emotional (FS):EOT(n= 28,42)	67.6 (± 25.19)	72.8 (± 22.62)		
Cognitive (FS):Baseline (n=45,70)	79.6 (± 20.38)	84.0 (± 20.74)		
Cognitive (FS):EOT(n=28,42)	69.6 (± 27.61)	77.4 (± 22.64)		
Social (FS):Baseline (n=45,70)	72.2 (± 29.94)	75.7 (± 27.02)		
Social (FS):EOT(n=28,42)	63.1 (± 27.35)	69.8 (± 24.76)		
Fatigue (SS):Baseline (n=45,70)	60.0 (± 22.89)	61.0 (± 23.07)		
Fatigue (SS):EOT(n=28,42)	50.8 (± 25.02)	50.3 (± 25.77)		
Nausea/Vomiting (SS):Baseline(n=45,70)	96.7 (± 8.41)	94.8 (± 11.54)		
Nausea/Vomiting (SS):EOT(n=28,42)	88.7 (± 15.75)	92.9 (± 16.52)		
Pain (SS):Baseline(n=45,70)	61.1 (± 30.77)	65.2 (± 24.70)		
Pain (SS): EOT(n=28,42)	51.2 (± 26.42)	53.2 (± 28.33)		
Dyspnea(SS):Baseline(n=45,70)	25.2 (± 28.56)	19.0 (± 25.74)		
Dyspnea (SS):EOT(n=28,42)	40.5 (± 30.57)	24.6 (± 26.61)		
Insomnia (SS):Baseline(n=45,70)	32.6 (± 29.72)	29.5 (± 31.87)		
Insomnia (SS):EOT(n=28,42)	36.9 (± 34.35)	29.4 (± 34.69)		
Appetite Loss (SS): Baseline(n=45,70)	22.2 (± 27.52)	14.3 (± 22.39)		
Appetite Loss (SS):EOT(n=28,42)	34.5 (± 34.52)	23.0 (± 28.02)		
Constipation (SS):Baseline(n=45,70)	13.3 (± 23.99)	11.4 (± 20.37)		
Constipation (SS):EOT(n=28,42)	25.0 (± 34.69)	19.8 (± 29.50)		
Diarrhea (SS):Baseline(n=45,70)	17.8 (± 23.14)	16.7 (± 23.23)		
Diarrhea (SS):EOT(n=28,42)	19.0 (± 26.34)	16.3 (± 25.95)		
Financial Difficulties (SS):Baseline(n=45,70)	22.2 (± 27.52)	17.1 (± 25.85)		
Financial Difficulties (SS):EOT(n=28,42)	16.7 (± 21.28)	12.7 (± 22.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQOL Based on EORTC Multiple Myeloma Module 20 (EORTC QLQ-MY20) Score

End point title	HRQOL Based on EORTC Multiple Myeloma Module 20 (EORTC QLQ-MY20) Score

End point description:

The EORTC QLQ-MY20 has 20 items across 4 independent subscales, 2 symptoms scales (disease symptoms, side effects of treatment), and 2 functional subscales (body image, future perspective). Scores were averaged and transformed to 0-100 scale. Higher scores for the future perspective scale

indicate better perspective of the future, for the body image scale indicate better body image and for the disease symptoms scale indicate higher level of symptomatology. ITT PRO Population included participants with a measurement at study entry and at least one post study entry measurement for at least 1 subscale on all 3 questionnaires (EORTC QLQ-C30, EORTC QLQ-MY20 and EQ-5D-5L). 'n' indicates number analysed are the number of participants with data available for analyses at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 28 cycles, each cycle was of 28 days)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	70		
Units: score on a scale				
arithmetic mean (standard deviation)				
Disease Symptoms: Baseline (n= 45, 70)	73.2 (± 17.06)	72.4 (± 21.31)		
Disease Symptoms: EOT (n= 28, 41)	73.5 (± 17.75)	68.9 (± 23.09)		
Side Effects of Treatment: Baseline (n= 45, 70)	81.0 (± 13.45)	81.4 (± 13.30)		
Side Effects of Treatment: EOT (n= 28, 41)	74.4 (± 17.84)	77.8 (± 14.47)		
Body Image: Baseline (n= 45, 70)	81.5 (± 23.09)	82.9 (± 23.90)		
Body Image: EOT (n= 28, 41)	75.0 (± 30.93)	83.7 (± 23.71)		
Future Perspective:Baseline(n=45,70)	58.8 (± 23.29)	67.5 (± 24.03)		
Future Perspective:EOT (n= 28, 41)	57.9 (± 28.26)	64.0 (± 19.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Responses to HRQOL Based on 5-level Classification System of the EuroQol 5-Dimensional Health Questionnaire (EQ-5D-5L) Score

End point title	Number of Participants with Responses to HRQOL Based on 5-level Classification System of the EuroQol 5-Dimensional Health Questionnaire (EQ-5D-5L) Score

End point description:

EQ-5D-5L comprises of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each rated on 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, 5= extremely severe problems. Higher scores indicated greater levels of problems across the five dimensions. ITT PRO Population included participants with a measurement at study entry and at least one post study entry measurement for at least 1 subscale on all 3 questionnaires (EORTC QLQ-C30, EORTC QLQ-MY20 and EQ-5D-5L). Overall number of participants analysed are the number of participants with data available for analyses. Self-Care – SC; Usual Activities - UA

End point type	Secondary

End point timeframe:

End of Treatment (Up to 28 cycles, each cycle was of 28 days)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	41		
Units: participants				
Mobility(M):1=I Have no Problems in Walking About	5	9		
M:2=I Have Slight Problems in Walking About	6	12		
M:3=I Have Moderate Problems in Walking About	8	11		
M:4=I Have Severe Problems in Walking About	8	8		
M:5=I am Unable to Walk About	0	1		
SC:1=I Have no Problems Washing or Dressing Myself	13	21		
SC:2= Have Slight Problems Washing/Dressing Myself	6	10		
SC:3=I Have Moderate Problems Washing/Dressing	5	4		
SC:4=I Have Severe Problems Washing/Dressing	3	4		
SC:5=I am Unable to Wash or Dress Myself	0	2		
UA:1=I Have no Problems Doing my UA	4	10		
UA:2=I Have Slight Problems Doing my UA	7	9		
UA:3=I Have Moderate Problems Doing my UA	8	12		
UA:4=I Have Severe Problems Doing my UA	7	7		
UA:5=I am Unable to do my UA	1	3		
Pain/Discomfort:1=I Have no Pain or Discomfort	3	8		
Pain/Discomfort:2=I Have Slight Pain or Discomfort	5	10		
Pain/Discomfort:3=I Have Moderate Pain/Discomfort	13	15		
Pain/Discomfort:4=I Have Severe Pain/Discomfort	6	6		
Pain/Discomfort:5=I Have Extreme Pain/Discomfort	0	2		
Anxiety/Depression:1=I Have no Pain/Discomfort	6	19		
Anxiety/Depression:2=I Have no Pain/Discomfort	8	13		
Anxiety/Depression:3=I Have no Pain/Discomfort	11	6		
Anxiety/Depression:4=I Have no Pain/Discomfort	2	1		
Anxiety/Depression:5=I Have no Pain/Discomfort	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQOL Based on EuroQol Visual Analogue Scale (EQ VAS) Score

End point title	HRQOL Based on EuroQol Visual Analogue Scale (EQ VAS) Score

End point description:

The EQ VAS records the respondent's self-rated health on a 20 centimeter (cm), vertical, visual analogue scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). The scores from all dimensions were combined into a single index score that was reported, where higher score was better quality of life. ITT PRO Population included participants with a measurement at study entry and at least one post study entry measurement for at least 1 subscale on all 3 questionnaires (EORTC QLQ-C30, EORTC QLQ-MY20 and EQ-5D-5L). 'n' indicates number analysed are the number of participants with data available for analyses at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Up to 28 cycles, each cycle was of 28 days)

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	70		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 45, 70)	59.2 (± 20.96)	64.4 (± 18.21)		
End of Treatment (n= 27, 41)	46.9 (± 19.07)	55.9 (± 19.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Utilization (HU): Number of Participants with at Least one Medical Encounter

End point title	Health Care Utilization (HU): Number of Participants with at Least one Medical Encounter

End point description:

Healthcare resources used during medical encounters included hospitalizations, emergency room stays, or outpatient visits. A hospitalization was defined as at least 1 overnight stay in an Intensive Care Unit and/or non-Intensive Care Unit (acute care unit, palliative care unit, and hospice). ITT Population included all participants who were randomised.

End point type	Secondary

End point timeframe:

Up to approximately 3 years

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: participants				
Hospitalizations	16	23		
Emergency Room Stays	9	11		
Outpatient Visits	29	32		

Statistical analyses

No statistical analyses for this end point

Secondary: HU: Duration of Medical Encounters

End point title	HU: Duration of Medical Encounters

End point description:

Duration of healthcare resources used during medical encounters including hospitalizations, emergency room stays, or outpatient visits was reported in days. A hospitalization was defined as at least 1 overnight stay in an Intensive Care Unit and/or non-Intensive Care Unit (acute care unit, palliative care unit, and hospice). ITT Population included all participants who were randomised.

End point type	Secondary

End point timeframe:

Up to approximately 3 years

End point values	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	73		
Units: days				
median (full range (min-max))				
Hospitalizations	2.0 (1.0 to 6.0)	1.0 (1.0 to 10.0)		
Emergency Room Stays	1.0 (1.0 to 3.0)	1.0 (1.0 to 3.0)		
Outpatient Visits	4.0 (1.0 to 57.0)	3.0 (1.0 to 34.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the informed consent up to 30 days after last dose of the study drug (Up to approximately 3 years)

Adverse event reporting additional description:

At each visit investigator had to document any occurrence of AEs,abnormal laboratory findings.Any event spontaneously reported by participant or observed by investigator was recorded,irrespective of relation to study treatment.All cause-mortality:all randomized participants(N=49,73).Serious+nonserious:Safety Population participants received>=1dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Pomalidomide 4 mg + Dexamethasone 40 mg

Reporting group description:

Pomalidomide 4 mg, capsules, orally, once daily on Days 1 to 21 of each 28-day cycle, plus dexamethasone 40 mg, (or 20 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 8, 15, and 22 of each 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Reporting group title	Ixazomib 4 mg + Dexamethasone 20 mg

Reporting group description:

Ixazomib 4 mg as starting dose, capsules, orally, once daily on Days 1, 8, and 15 of each 28-day cycle, with escalation to 5.5 mg at the start of Cycle 2 for participants who tolerated the 4 mg dose in Cycle 1, plus dexamethasone 20 mg (or 10 mg if participant is aged >=75 years), tablets, orally, once daily on Days 1, 2, 8, 9, 15, 16, 22, and 23 of every 28-day cycle until disease progression, unacceptable toxicity, withdrawal of consent, or sponsor termination of study up to 2 years.

Serious adverse events	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 47 (53.19%)	37 / 72 (51.39%)	
number of deaths (all causes)	15	29	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	3 / 47 (6.38%)	4 / 72 (5.56%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 2	
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage II			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 47 (2.13%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pyrexia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Facial pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 47 (4.26%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung consolidation			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Enterobacter test positive			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Scrotal haematoma			

subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 47 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomegaly			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 47 (2.13%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			

subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 47 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	0 / 47 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Ileus			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			

subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Crystal arthropathy			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthralgia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	10 / 47 (21.28%)	9 / 72 (12.50%)	
occurrences causally related to treatment / all	2 / 13	3 / 14	
deaths causally related to treatment / all	0 / 2	0 / 3	
Bronchitis			
subjects affected / exposed	0 / 47 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 47 (2.13%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 47 (2.13%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			

subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 47 (2.13%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection fungal			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	2 / 47 (4.26%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 47 (0.00%)	3 / 72 (4.17%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pomalidomide 4 mg + Dexamethasone 40 mg	Ixazomib 4 mg + Dexamethasone 20 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 47 (95.74%)	62 / 72 (86.11%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 47 (6.38%)	1 / 72 (1.39%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 47 (23.40%)	17 / 72 (23.61%)	
occurrences (all)	13	21	
Asthenia			

subjects affected / exposed	8 / 47 (17.02%)	4 / 72 (5.56%)	
occurrences (all)	12	5	
Pyrexia			
subjects affected / exposed	6 / 47 (12.77%)	3 / 72 (4.17%)	
occurrences (all)	10	3	
Oedema peripheral			
subjects affected / exposed	2 / 47 (4.26%)	10 / 72 (13.89%)	
occurrences (all)	3	12	
Influenza like illness			
subjects affected / exposed	3 / 47 (6.38%)	1 / 72 (1.39%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	5 / 47 (10.64%)	4 / 72 (5.56%)	
occurrences (all)	5	4	
Cough			
subjects affected / exposed	6 / 47 (12.77%)	4 / 72 (5.56%)	
occurrences (all)	6	4	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 47 (10.64%)	16 / 72 (22.22%)	
occurrences (all)	6	16	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	3 / 47 (6.38%)	1 / 72 (1.39%)	
occurrences (all)	5	2	
Platelet count decreased			
subjects affected / exposed	4 / 47 (8.51%)	9 / 72 (12.50%)	
occurrences (all)	7	17	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 47 (2.13%)	5 / 72 (6.94%)	
occurrences (all)	1	5	
Nervous system disorders			
Peripheral sensory neuropathy			

subjects affected / exposed	3 / 47 (6.38%)	19 / 72 (26.39%)	
occurrences (all)	3	27	
Dizziness			
subjects affected / exposed	3 / 47 (6.38%)	5 / 72 (6.94%)	
occurrences (all)	3	5	
Headache			
subjects affected / exposed	0 / 47 (0.00%)	4 / 72 (5.56%)	
occurrences (all)	0	5	
Tremor			
subjects affected / exposed	3 / 47 (6.38%)	1 / 72 (1.39%)	
occurrences (all)	4	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 47 (38.30%)	12 / 72 (16.67%)	
occurrences (all)	29	15	
Thrombocytopenia			
subjects affected / exposed	8 / 47 (17.02%)	16 / 72 (22.22%)	
occurrences (all)	13	29	
Neutropenia			
subjects affected / exposed	19 / 47 (40.43%)	1 / 72 (1.39%)	
occurrences (all)	32	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	13 / 47 (27.66%)	28 / 72 (38.89%)	
occurrences (all)	14	43	
Nausea			
subjects affected / exposed	7 / 47 (14.89%)	12 / 72 (16.67%)	
occurrences (all)	8	13	
Constipation			
subjects affected / exposed	8 / 47 (17.02%)	9 / 72 (12.50%)	
occurrences (all)	8	9	
Vomiting			
subjects affected / exposed	4 / 47 (8.51%)	10 / 72 (13.89%)	
occurrences (all)	6	10	
Abdominal pain upper			

subjects affected / exposed	3 / 47 (6.38%)	2 / 72 (2.78%)	
occurrences (all)	3	2	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 47 (10.64%)	0 / 72 (0.00%)	
occurrences (all)	5	0	
Rash maculo-papular			
subjects affected / exposed	1 / 47 (2.13%)	4 / 72 (5.56%)	
occurrences (all)	1	4	
Dry skin			
subjects affected / exposed	0 / 47 (0.00%)	4 / 72 (5.56%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 47 (4.26%)	8 / 72 (11.11%)	
occurrences (all)	2	8	
Bone pain			
subjects affected / exposed	4 / 47 (8.51%)	6 / 72 (8.33%)	
occurrences (all)	4	6	
Muscular weakness			
subjects affected / exposed	4 / 47 (8.51%)	6 / 72 (8.33%)	
occurrences (all)	5	10	
Pain in extremity			
subjects affected / exposed	3 / 47 (6.38%)	6 / 72 (8.33%)	
occurrences (all)	3	7	
Muscle spasms			
subjects affected / exposed	4 / 47 (8.51%)	4 / 72 (5.56%)	
occurrences (all)	4	4	
Arthralgia			
subjects affected / exposed	3 / 47 (6.38%)	3 / 72 (4.17%)	
occurrences (all)	3	3	
Musculoskeletal pain			
subjects affected / exposed	1 / 47 (2.13%)	4 / 72 (5.56%)	
occurrences (all)	1	4	
Infections and infestations			

Upper respiratory tract infection			
subjects affected / exposed	6 / 47 (12.77%)	7 / 72 (9.72%)	
occurrences (all)	8	10	
Bronchitis			
subjects affected / exposed	6 / 47 (12.77%)	6 / 72 (8.33%)	
occurrences (all)	8	9	
Urinary tract infection			
subjects affected / exposed	6 / 47 (12.77%)	3 / 72 (4.17%)	
occurrences (all)	16	3	
Pneumonia			
subjects affected / exposed	4 / 47 (8.51%)	4 / 72 (5.56%)	
occurrences (all)	4	4	
Nasopharyngitis			
subjects affected / exposed	3 / 47 (6.38%)	3 / 72 (4.17%)	
occurrences (all)	3	4	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 47 (4.26%)	5 / 72 (6.94%)	
occurrences (all)	3	5	
Decreased appetite			
subjects affected / exposed	4 / 47 (8.51%)	2 / 72 (2.78%)	
occurrences (all)	5	2	
Hyperglycaemia			
subjects affected / exposed	1 / 47 (2.13%)	5 / 72 (6.94%)	
occurrences (all)	1	5	
Hypomagnesaemia			
subjects affected / exposed	4 / 47 (8.51%)	1 / 72 (1.39%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2019	Amendment 5: Summary of changes: The primary purpose of this amendment was to make following changes: - To conclude the study following the phase 2 portion of the study and not initiate the previously planned phase 3 portion of the study. This change in study design was in response to an assessment of the current landscape of myeloma treatments and a slower rate of efficacy event accumulation than projected in the original study design. - The testing strategy was updated to have a single study analysis, to occur when approximately 80 PFS events were observed, and, correspondingly, to update the PFS assumption and type I error control allocation.
31 August 2020	Amendment 6: Summary of changes: The primary purpose of this amendment was to make following changes: - Modified the study assessments as the data cutoff date for the study analysis had been reached (31 May 2020). - Only participants who continued to demonstrate clinical benefit but who did not have other means of access to the study drugs continued on the study. Because no further formal statistical analyses were performed, only assessments contributing to long-term safety data were required. Most study assessments besides safety were discontinued to ease the burden of protocol-mandated assessments on participants. Added flexibility in study conduct in unavoidable circumstances (e.g., the COVID-19 pandemic).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported