Clinical trial results:
A Phase 3 Randomised, Open-label, Multicenter Study Comparing Isatuximab (SAR650984) in Combination with Pomalidomide and Low-dose Dexamethasone versus Pomalidomide and Low-dose Dexamethasone in Patients with Refractory or Relapsed and Refractory Multiple Myeloma

Summary

EudraCT number	2016-003097-41
Trial protocol	SE HU PT ES CZ NO GB SK BE DK FR GR DE PL IT
Global end of trial date	

Results information

Result version number	v4 (current)
This version publication date	08 February 2025
First version publication date	17 April 2020
Version creation reason	• Correction of full data set Align with ClinicalTrials.gov

Trial information

Trial identification

Sponsor protocol code	EFC14335

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02990338
WHO universal trial number (UTN)	U1111-1180-6262
Other trial identifiers	Study Name: ICARIA-MM

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 Avenue Pierre Brossolette, Chilly Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	14 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 November 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the benefit of isatuximab in combination with pomalidomide and low-dose dexamethasone in the prolongation of Progression Free Survival (PFS) as compared to pomalidomide and low-dose dexamethasone in subjects with refractory or relapsed and refractory multiple myeloma (MM).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject was participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	New Zealand: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Czechia: 28
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 49
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Slovakia: 1

Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Türkiye: 36
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 9
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Russian Federation: 13
Worldwide total number of subjects	307
EEA total number of subjects	174

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)	124
From 65 to 84 years	180
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 102 sites in 24 countries. A total of 387 subjects were screened between 22 December 2016 and 01 February 2018. Out of which, 307 subjects were randomised in 1:1 ratio to IPd (Isatuximab + Pomalidomide + Dexamethasone) and Pd (Pomalidomide + Dexamethasone) arms using an interactive response technology (IRT).

Pre-assignment

Screening details:

Randomisation stratified by age (less than [<] 75 years versus greater than and equal to [>=] 75 years) and number of previous lines of therapy (2 or 3 versus more than 3). "Reason for not completed" = "Reason for definitive treatment discontinuation."

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	Pd (Pomalidomide + Dexamethasone)

Arm description:

Subjects received pomalidomide 4 milligrams (mg) Per os (PO) on Days 1 to 21 of each 28-day treatment cycle plus dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone) PO on Days 1, 8, 15 and 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject’s wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 306.6 weeks).

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

40 mg (or 20 mg if the subject was >=75 years old), PO or Intravenous (IV) was given on Days 1, 8, 15 and 22 of each 28-day treatment cycle.

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

Dosage and administration details:

4 mg PO on Days 1 to 21 of each 28-day treatment cycle.

Arm title	IPd (Isatuximab + Pomalidomide + Dexamethasone)

Arm description:

Subjects received isatuximab 10 milligrams per kilogram (mg/kg) IV infusion on Days 1, 8, 15, and 22 at Cycle 1, and then on Days 1 and 15 of subsequent cycles plus pomalidomide 4 mg PO on Days 1 to 21 of each 28-day treatment cycle and dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone), PO or IV on Day 1, 8, 15, 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject’s wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 311.0 weeks).

Arm type	Experimental

Investigational medicinal product name	Isatuximab
Investigational medicinal product code	SAR650984
Other name	Sarclisa
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg IV infusion administered on Days 1, 8, 15, and 22 for the first cycle and then Days 1 and 15 of each 28-day treatment cycle.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

40 mg (or 20 mg if the subject was >=75 years old), PO or IV was given on Days 1, 8, 15 and 22 of each 28-day treatment cycle.

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

Dosage and administration details:

4 mg PO on Days 1 to 21 of each 28-day treatment cycle.

Number of subjects in period 1	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)
Started	153	154
Treated	149	152
Completed	0	0
Not completed	153	154
Consent withdrawn by subject	6	8
Randomized and not treated	4	2
Adverse event	23	22
Unconfirmed disease progression per investigator	-	1
Poor compliance to protocol	-	1
Treatment extension study	-	6
Progressive disease	118	107
Continue with therapy available commercially	-	1
Physician's decision	2	6

Baseline characteristics

Reporting groups	
Reporting group title	Pd (Pomalidomide + Dexamethasone)
Reporting group description:	
Subjects received pomalidomide 4 milligrams (mg) Per os (PO) on Days 1 to 21 of each 28-day treatment cycle plus dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone) PO on Days 1, 8, 15 and 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 306.6 weeks).	
Reporting group title	IPd (Isatuximab + Pomalidomide + Dexamethasone)
Reporting group description:	
Subjects received isatuximab 10 milligrams per kilogram (mg/kg) IV infusion on Days 1, 8, 15, and 22 at Cycle 1, and then on Days 1 and 15 of subsequent cycles plus pomalidomide 4 mg PO on Days 1 to 21 of each 28-day treatment cycle and dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone), PO or IV on Day 1, 8, 15, 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 311.0 weeks).	

Reporting group values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)	Total
Number of subjects	153	154	307
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65.2	66.6	
standard deviation	± 9.5	± 9.1	-
Gender categorical Units: Subjects			
Female	83	65	148
Male	70	89	159
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	15	21	36
Native Hawaiian or Other Pacific Islander	1	2	3
Black or African American	3	1	4
White	126	118	244
More than one race	0	0	0
Unknown or Not Reported	8	12	20

End points

End points reporting groups

Reporting group title	Pd (Pomalidomide + Dexamethasone)

Reporting group description:

Subjects received pomalidomide 4 milligrams (mg) Per os (PO) on Days 1 to 21 of each 28-day treatment cycle plus dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone) PO on Days 1, 8, 15 and 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 306.6 weeks).

Reporting group title	IPd (Isatuximab + Pomalidomide + Dexamethasone)

Reporting group description:

Subjects received isatuximab 10 milligrams per kilogram (mg/kg) IV infusion on Days 1, 8, 15, and 22 at Cycle 1, and then on Days 1 and 15 of subsequent cycles plus pomalidomide 4 mg PO on Days 1 to 21 of each 28-day treatment cycle and dexamethasone 40 mg (subjects >= 75 years of age received 20 mg dexamethasone), PO or IV on Day 1, 8, 15, 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or subject's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 311.0 weeks).

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS: time from date of randomisation to date of first documentation of progressive disease (PD) determined by Independent Response Committee(IRC) or date of death from any cause, whichever comes first. If progression or death was not observed, subject was censored at date of last progression-free tumor assessment prior to study cut-off date and initiation of further anti-myeloma treatment (if any). Analysis performed by Kaplan-Meier method. PD as per International Myeloma Working Group (IMWG) criteria, defined as increase of >=25% from lowest confirmed value in serum M protein (absolute increase must be >=0.5g/dL or >=1g/dL if lowest M component was >=5g/dL) or urine M-protein (absolute increase must be >=200mg/24hour), appearance of new lesion(s),>=50%increase from nadir in sum of the products of the maximal perpendicular diameters of measured lesions (SPD), or >=50% increase in longest diameter of a previous lesion >1 centimeter in short axis. Intent-to-treat (ITT) population.

End point type	Primary

End point timeframe:

From the date of randomisation to the date of first documentation of progression, or the date of death from any cause, or initiation of further anti-myeloma treatment or data cut-off whichever comes first (maximum duration: 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: months				
median (confidence interval 95%)	6.47 (4.468 to 8.279)	11.53 (8.936 to 13.897)		

Statistical analyses

Statistical analysis title	Statistical Analysis for PFS

Statistical analysis description:

Confidence interval (CI) for Kaplan-Meier estimates were calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley.

Comparison groups	Pd (Pomalidomide + Dexamethasone) v IPd (Isatuximab + Pomalidomide + Dexamethasone)
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0005 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.596
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.436
upper limit	0.814

Notes:

[1] - A closed test procedure was used to control the type I error rate meaning no further testing would be performed unless the significance level had been reached on PFS.
[2] - One-sided p-value based on Stratified log-rank test. Threshold for statistical significance at 0.025. Stratification was based on age (<75 years versus >=75 years) and number of previous lines of therapy (2 or 3 versus >3) according to IRT.

Secondary: Overall Response Rate (ORR): Percentage of Subjects With Disease Response as Per Independent Response Committee (IRC)

End point title	Overall Response Rate (ORR): Percentage of Subjects With Disease Response as Per Independent Response Committee (IRC)

End point description:

ORR (IMWG criteria): percentage of subjects with stringent complete response(sCR), complete response(CR),very good partial response(VGPR), and partial response(PR) as best overall response, assessed by IRC. sCR:negative immunofixation on serum and urine,disappearance of any soft tissue plasmacytomas,<5% plasma cells in bone marrow aspirates plus normal free light chain(FLC)ratio(0.26-1.65), absence of clonal cells in bone marrow biopsy.CR:negative immunofixation on serum and urine,disappearance of any soft tissue plasmacytomas,<5% plasma cells in bone marrow aspirates.VGPR: serum and urine M-protein detectable by immunofixation, not on electrophoresis/,>=90% reduction in serum M-protein plus urine M-protein level <100mg/24h/,>=90% decrease in SPD compared to baseline in soft tissue plasmacytoma. PR: >=50% reduction of serum M-protein and reduction in 24h urinary M-protein by >=90%/<200mg/24h,if present at baseline,>=50% reduction in the size(SPD) of soft tissue plasmacytomas. ITT.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documentation of progression or initiation of further anti-myeloma treatment or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: percentage of subjects				
number (not applicable)	35.3	60.4		

Statistical analyses

Statistical analysis title	Statistical Analysis for ORR
Comparison groups	Pd (Pomalidomide + Dexamethasone) v IPd (Isatuximab + Pomalidomide + Dexamethasone)
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - A closed test procedure was used to control the type I error rate meaning no further testing would be performed unless the significance level had been reached on PFS.
[4] - Threshold for statistical significance at 0.025. One sided p-value was stratified based on age (<75 years versus >=75 years) and number of previous lines (2 or 3 versus >3) according to IRT.

Secondary: Percentage of Subjects With Best Overall Response (BOR) as Per Independent Response Committee

End point title	Percentage of Subjects With Best Overall Response (BOR) as Per Independent Response Committee

End point description:

BOR:best sequential response from start of treatment until disease progression,death, initiation of further anti-myeloma treatment/data cut-off,whichever comes first.Ordering of evaluations from best to worse was: sCR,CR,VGPR,PR, minimal response(MR), stable disease(SD),PD, and not evaluable.CR:negative immunofixation on serum and urine,disappearance of any soft tissue plasmacytomas,<5% plasma cells in bone marrow aspirates. sCR:CR as defined previously plus normal FLC ratio(0.26 to 165),absence of clonal cells in bone marrow biopsy.VGPR:serum and urine M-protein detectable by immunofixation,>=90% reduction in serum M-protein plus urine M-protein level <100mg/24h,>=90% decrease in SPD compared to baseline in soft tissue plasmacytoma. PR:>=50% reduction of serum M-protein and reduction in 24h urinary M-protein by >=90%/<200mg/24h. MR:>=25% but <=49% reduction in serum M-protein and reduction in 24h urine M-protein by 50-89%. SD:Not meeting criteria for CR,VGPR,PR,MR/PD. ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation until disease progression, or death, initiation of further anti-myeloma treatment or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: percentage of subjects				
number (not applicable)				
Stringent complete response	0.7	0		
Complete response	1.3	4.5		
Very good partial response	6.5	27.3		
Partial response	26.8	28.6		
Minimal response	11.1	6.5		
Stable disease	29.4	21.4		
Progressive Disease	9.2	3.9		
Not evaluable	10.5	4.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Very Good Partial Response (VGPR) as Per Independent Response Committee

End point title	Percentage of Subjects With Very Good Partial Response (VGPR) as Per Independent Response Committee

End point description:

VGPR rate was defined as the percentage of subjects achieving a VGPR or better as BOR. VGPR was defined as serum and urine M-protein detectable by immunofixation but not on electrophoresis or >=90% reduction in serum M-protein plus urine M-protein level <100 mg/24 h or >=90% decrease in the sum of maximal perpendicular diameter compared to baseline in soft tissue plasmacytoma. BOR was defined as the best sequential response (CR), using the IRC's assessment of response, from the start of treatment until disease progression (provided that the progression is subsequently confirmed in case of progression requiring confirmation), death, initiation of further anti-myeloma treatment, or cut-off date, whichever occurs first. CR: negative immunofixation on serum and urine, disappearance of any soft tissue plasmacytomas,<5% plasma cells in bone marrow aspirates. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documentation of progression, death, initiation of further antimyeloma treatment, or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: percentage of subjects				

number (not applicable)	8.5	31.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR): Percentage of Subjects With Clinical Benefit as Per Independent Response Committee

End point title	Clinical Benefit Rate (CBR): Percentage of Subjects With Clinical Benefit as Per Independent Response Committee

End point description:

CBR was defined as the percentage of subjects achieving a MR or better as BOR. MR was defined as >= 25% but <= 49% reduction in serum M-protein and reduction in 24h urine M-protein by 50-89%, which still exceed 200 mg/24h; if present at baseline, >=50% reduction in size (SPD) of soft tissue plasmacytomas was also required. BOR was defined as the best sequential response, using the IRC's assessment of response, from the start of treatment until disease progression (provided that the progression is subsequently confirmed in case of progression requiring confirmation), death, initiation of further anti-myeloma treatment, or cut-off date, whichever occurs first. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documentation of progression, death, initiation of further antimyeloma treatment or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: percentage of subjects				
number (not applicable)	46.4	66.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS): Final Analysis

End point title	Overall Survival (OS): Final Analysis

End point description:

OS was defined as the time from the date of randomisation to death from any cause. In the absence of confirmation of death, survival time was censored at the last date subject was known to be alive or at the cut-off date, whichever comes first. This pre-specified final analysis was performed when the 220 OS events were met. Analysis was performed on ITT population which included all randomised subjects.

End point type	Secondary

End point timeframe:

From the date of randomisation to date of death from any cause or data cut-off date, whichever was earlier (maximum duration 245.6 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: months				
median (confidence interval 95%)	17.71 (14.390 to 26.218)	24.57 (20.304 to 31.310)		

Statistical analyses

Statistical analysis title	Statistical Analysis for OS: Final Analysis
Comparison groups	Pd (Pomalidomide + Dexamethasone) v IPd (Isatuximab + Pomalidomide + Dexamethasone)
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0319 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.776
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.594
upper limit	1.015

Notes:

[5] - A closed test procedure was used to control the type I error rate meaning no further testing would be performed unless the significance level had been reached on PFS.
[6] - One-sided significance level was 0.02 using the O'Brien-Fleming alpha spending function. Stratified on age (<75 years versus >=75 years) and number of previous lines of therapy (2 or 3 versus > 3) according to IRT.

Secondary: Time to Progression (TTP) as Per Independent Response Committee

End point title	Time to Progression (TTP) as Per Independent Response Committee

End point description:

TTP was defined as time from randomisation to the date of first documentation of PD, as determined by the IRC. As per IMWG criteria, PD was defined for subjects with increase of >= 25% from lowest confirmed value in any one of the following criteria: serum M-protein (the absolute increase must be >= 0.5 g/dL), serum M-protein increase >=1 g/dL if the lowest M component was >=5 g/dL; urine M-component (the absolute increase must be >=200 mg/24hour), appearance of new lesion(s), >=50% increase from nadir in SPD of >1 lesion, or >=50% increase in the longest diameter of a previous lesion >1 centimetre in short axis. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documentation of progression, or initiation of further anti-myeloma treatment or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: months				
median (confidence interval 95%)	7.75 (5.027 to 9.758)	12.71 (11.203 to 15.211)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival in High Risk Cytogenetic Population

End point title	Progression Free Survival in High Risk Cytogenetic Population

End point description:

PFS in high risk cytogenetic population was defined as PFS in subgroup of subjects carrying high risk cytogenetic changes including del(17p), translocation (t)(4;14) or t(14;16) assessed by fluorescence in situ hybridisation (FISH). PFS was defined as the time from date of randomisation to date of first documentation of PD (determined by IRC) or date of death from any cause, whichever comes first. PD defined as per IMWG criteria as: increase of >=25% from lowest confirmed value in any one of following criteria:serum M-protein (absolute increase must be >=0.5 g/dL), serum M-protein increase >=1g/dL if lowest M component was >=5 g/dL;urine M-component (absolute increase must be >=200 mg/24hour), appearance of new lesion(s),>=50% increase from nadir in SPD of >1 lesion, or >=50% increase in the longest diameter of previous lesion >1 cm in short axis. Analysis performed in high-risk cytogenetic population which included subjects carrying del (17p), t(4;14) or t(14;16) in each arm.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documentation of progression, or the date of death from any cause, or initiation of further anti-myeloma treatment or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	25[7]		
Units: months				
median (confidence interval 95%)	3.745 (2.793 to 7.885)	7.491 (2.628 to 99999)		

Notes:

[7] - '99999' was used as due to smaller number of subjects with an event, 95% CI could not be calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Per Independent Response Committee

End point title	Duration of Response (DOR) as Per Independent Response Committee

End point description:

DOR: time from date of first IRC determined response(PR or better) to date of first IRC-PD or death, whichever occurred first. DOR was determined only for subjects who had achieved a response of PR or better based on disease assessment by IRC. If progression or death was not observed, subject was censored at date of subject's last progression-free tumor assessment prior to initiation of further anti-myeloma treatment(if any)and study cut-off date. PD (IMWG criteria): increase of >=25% from lowest confirmed value in serum M-protein (absolute increase must be >=0.5 g/dL), serum M-protein increase >=1g/dL if lowest M component was >=5g/dL;urine M-component (absolute increase must be >=200mg/24h),appearance of new lesion(s), >=50% increase from nadir in SPD of >1 lesion,or >=50% increase in the longest diameter of a previous lesion >1 cm in short axis. PR:>=50% reduction of serum M-protein and reduction in 24h urinary M-protein by >=90%/<200mg/24h. Responders in ITT population.

End point type	Secondary

End point timeframe:

From the date of the first IRC determined response to the date of first IRC progression or death, whichever occurred first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[8]	93[9]		
Units: months				
median (confidence interval 95%)	11.07 (8.542 to 99999)	13.27 (10.612 to 99999)		

Notes:

[8] - '99999' was used as due to smaller number of subjects with an event, 95% CI could not be calculated.
[9] - '99999' was used as due to smaller number of subjects with an event, 95% CI could not be calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Response (TT1R) as Per Independent Response Committee

End point title	Time to First Response (TT1R) as Per Independent Response Committee

End point description:

TT1R was defined as the time from randomisation to the date of first IRC determined response (PR or better) that is subsequently confirmed. PR was defined as >=50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by >=90% or to <200 mg/24 h. In addition to the above listed criteria, if present at baseline, a >=50% reduction in the size (SPD) of soft tissue plasmacytomas was also required. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first IRC determined response, or death or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: months				
median (confidence interval 95%)	3.02 (2.825 to 5.060)	1.94 (1.314 to 2.004)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Best Response (TTBR) as Per Independent Response Committee

End point title	Time to Best Response (TTBR) as Per Independent Response Committee

End point description:

TTBR was defined as the time from randomisation to the date of first occurrence of IRC determined BOR (PR or better) that was subsequently confirmed. PR was defined as >=50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by >=90% or to <200 mg/24 h. In addition to the above listed criteria, if present at baseline, a >=50% reduction in the size (SPD) of soft tissue plasmacytomas was also required. BOR was defined as the best sequential response, using the IRC's assessment of response, from the start of treatment until disease progression (provided that the progression is subsequently confirmed in case of progression requiring confirmation), death, initiation of further anti-myeloma treatment, or cut-off date, whichever occurs first. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

From the date of randomisation to date of first occurrence of IRC determined best overall response or data cut-off whichever comes first (maximum duration 76.7 weeks)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: months				
median (confidence interval 95%)	5.06 (3.778 to 7.885)	4.30 (2.891 to 5.125)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Minimal Residual Disease (MRD)

End point title	Number of Subjects With Minimal Residual Disease (MRD)

End point description:

MRD was assessed by next-generation sequencing in bone marrow samples from subjects who achieved CR, to determine the depth of response at the molecular level. IMWG criteria for CR: Negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas, and <5% plasma cells in bone marrow aspirates. MRD was classified as positive or negative at the minimum sensitivity of 1 in 10^5 nucleated cells. MRD negativity was defined as the absence of the dominant clonotype sequence(s) identified in the bone marrow aspirate collected at screening. MRD positivity was defined as the presence of the dominant clonotype sequence(s) identified in the bone marrow aspirate collected at screening. Analysis was performed on ITT population who were evaluable for MRD.

End point type	Secondary

End point timeframe:

Up to 76.7 weeks

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	14		
Units: subjects				
number (not applicable)				
MRD negative:1 in 10^4	0	10		
MRD negative:1 in 10^5	0	8		
MRD negative:1 in 10^6	0	2		
MRD positive:1 in 10^4	2	4		
MRD positive:1 in 10^5	2	6		
MRD positive:1 in 10^6	2	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

Adverse Event (AE) was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had a causal relationship with the treatment. TEAEs were defined as AEs that developed, worsened (according to the Investigator opinion), or became serious during the treatment period (time from the first dose of study treatments up to 30 days after last dose of study treatments). An SAE is any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability / incapacity, was a congenital anomaly / birth defect, was a medically important event. Analysis was performed on safety population which included all subjects from the ITT population who received at least one dose or a part of a dose of the study treatments.

End point type	Secondary

End point timeframe:

From randomisation up to 30 days after last dose of study drug (maximum duration up to 241.6 weeks for Pd arm and 245.6 weeks for IPd arm)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	152		
Units: subjects				
number (not applicable)				
Any TEAE	146	151		
Any treatment emergent SAE	91	112		
Any TEAE leading to treatment discontinuation	22	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) Parameter: Plasma Concentration of Isatuximab at End of Infusion (CEOI)

End point title	Pharmacokinetics (PK) Parameter: Plasma Concentration of Isatuximab at End of Infusion (CEOI)[10]

End point description:

CEOI was defined as the plasma concentration at end of infusion. Analysis was performed on PK population which included subjects who received at least 1 dose of Isatuximab, with data for at least 1 PK parameter available. Here, 'n' signifies subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

End of infusion on Cycle(C)1 Day(D)1 and Cycle1 Day 15; Cycle 2 Day 1; and Cycle 4 Day 1

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: microgram per millilitre (mcg/mL)				
geometric mean (geometric coefficient of variation)				
End of infusion: C1D1 (n=141)	163.05 (± 34.528)			
End of infusion: C1D15 (n=120)	269.20 (± 32.622)			
End of infusion: C2D1 (n=134)	299.85 (± 35.921)			
End of infusion: C4D1 (n=117)	279.31 (± 47.555)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Accumulation Ratio of Isatuximab at Concentration at the End of Infusion (CEOI)

End point title	Pharmacokinetic Parameter: Accumulation Ratio of Isatuximab at Concentration at the End of Infusion (CEOI)[11]

End point description:

Accumulation Ratio was defined as the ratio of CEOI of Cycle 2 Day 1 versus Cycle 1 Day 1 and Cycle 4 Day 1 versus Cycle 1 Day 1, where CEOI was the plasma concentration at the end of infusion. Analysis was performed on PK population. Here, 'n' signifies subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

End of infusion on Cycle 1 Day 1, Cycle 2 Day 1, and Cycle 4 Day 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: ratio				
geometric mean (geometric coefficient of variation)				
C2D1 versus C1D1 (n=130)	1.860 (± 170.9185)			
C4D1 versus C1D1 (n=112)	1.777 (± 224.2542)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Plasma Concentration of Isatuximab at 1 Hour After End of Infusion (CEOI+1 Hour)

End point title	Pharmacokinetic Parameter: Plasma Concentration of Isatuximab at 1 Hour After End of Infusion (CEOI+1 Hour)[12]

End point description:

CEOI+1 hour was defined as the plasma concentration of isatuximab at 1 hour after end of infusion. Analysis was performed on PK population. Here, 'n' signifies subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Cycle 1:1 hour after End of Infusion on Day 1; Cycle 4:1 hour after End of Infusion on Day 1

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=140)	171.55 (± 38.299)			
C4D1 (n=114)	294.96 (± 57.331)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Plasma Concentration of Isatuximab at Ctrough

End point title	PK Parameter: Plasma Concentration of Isatuximab at

End point description:

Trough Concentration (Ctrough) is the concentration prior to study drug administration. Analysis was performed on PK population. Here, 'n' signifies subjects with available data for each specified category and '99999' is used as space fillers as due to smaller number of subjects with an event, geometric CV% could not be calculated.

End point type	Secondary

End point timeframe:

Pre-infusion on C1D1, C1D8, C1D15, C1D22, C2D1, C2D15, C3D1, C3D15, C4D1, C4D15, C5D1, C6D1, C7D1, C8D1, C9D1, C10D1, C11D1, C12D1, C13D1, C14D1, C15D1, C16D1, C17D1, C18D1, C19D1, C20D1; End of treatment (EOT[30 days after last drug administration])

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)				
C1D1 (n=144)	0.00 (± 1194.973)			
C1D8 (n=135)	31.49 (± 53.602)			
C1D15 (n=126)	57.89 (± 54.764)			
C1D22 (n=126)	84.82 (± 57.666)			
C2D1 (n=138)	89.09 (± 60.155)			
C2D15 (n=121)	89.35 (± 61.167)			
C3D1 (n=131)	64.15 (± 76.469)			
C3D15 (n=109)	91.73 (± 78.406)			
C4D1 (n=118)	86.05 (± 70.062)			
C4D15 (n=108)	105.42 (± 68.035)			
C5D1 (n=108)	106.08 (± 65.275)			
C6D1 (n=107)	111.33 (± 64.985)			
C7D1 (n=96)	134.14 (± 60.017)			

C8D1 (n=86)	146.15 (± 55.946)			
C9D1 (n=82)	162.84 (± 65.193)			
C10D1 (n=73)	145.86 (± 60.719)			
C11D1 (n=71)	169.39 (± 56.078)			
C12D1 (n=63)	182.32 (± 56.814)			
C13D1 (n=49)	215.85 (± 54.667)			
C14D1 (n=35)	214.88 (± 55.172)			
C15D1 (n=24)	253.61 (± 58.885)			
C16D1 (n=19)	206.60 (± 50.965)			
C17D1 (n=13)	242.79 (± 45.364)			
C18D1 (n=8)	216.70 (± 58.273)			
C19D1 (n=5)	240.36 (± 42.099)			
C20D1 (n=1)	164.07 (± 99999)			
EOT (n=60)	9.51 (± 136.883)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Accumulation Ratio of Isatuximab at Trough Concentration (Ctrough)

End point title	PK Parameter: Accumulation Ratio of Isatuximab at Trough Concentration (Ctrough)[14]

End point description:

Accumulation Ratio was defined as the ratio of Ctrough of Cycle 2 Day 1 versus Cycle 1 Day 8 and Cycle 4 Day 1 versus Cycle 1 Day 8, where Ctrough is the concentration prior to study drug administration. Analysis was performed on PK population. Here, 'n' signifies subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-infusion on Cycle 1 Day 8, Cycle 2 Day 1 and Cycle 4 Day 1

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	149			
Units: ratio				
geometric mean (geometric coefficient of variation)				
C2D1 versus C1D8 (n=125)	2.689 (± 734.5547)			
C4D1 versus C1D8 (n=108)	2.620 (± 645.4171)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Cancer Specific Questionnaire With 30 Items (EORTC QLQ-C30): Global Health Status (GHS)/Quality of Life (QOL) Score

End point title	Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Cancer Specific Questionnaire With 30 Items (EORTC QLQ-C30): Global Health Status (GHS)/Quality of Life (QOL) Score

End point description:

EORTC-Quality of Life Questionnaire (QLQ)-C30 is a cancer-specific instrument with 30 questions for evaluation of new chemotherapy and provides an assessment of subject reported outcome dimensions. EORTC QLQ-C30 included GHS/ QOL, functional scales (physical, role, cognitive, emotional, social), symptom scales (fatigue, pain, nausea/ vomiting), and 6 single items (dyspnea, appetite loss, insomnia, constipation, diarrhoea, financial difficulties). Most questions from QLQ-C30 were a 4-point scale (1/Not at All to 4/Very Much), except Items 29-30, which comprise GHS scale and were a 7-point scale (1/Very Poor to 7/Excellent). Answers were converted into grading scale, with values between 0 and 100. A high score represented a favorable outcome with a best quality of life for subject. Analysis was performed on safety population evaluable for global health status. Here, 'n' signifies subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (Cycle 3, Cycle 6, Cycle 9, and Cycle 17)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	139		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=134,137)	61.19 (± 20.64)	60.10 (± 20.02)		

Day 1: Cycle 3 (n=109,123)	-1.45 (± 21.03)	-1.22 (± 22.42)		
Day 1: Cycle 6 (n=69,102)	-0.12 (± 22.26)	-0.16 (± 18.28)		
Day 1: Cycle 9 (n=55,82)	1.06 (± 19.97)	0.41 (± 20.99)		
Day 1: Cycle 17 (n=10,13)	-9.17 (± 24.36)	-1.92 (± 19.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-drug Antibodies (ADA)

End point title	Number of Subjects With Anti-drug Antibodies (ADA)[15]

End point description:

ADA were categorised as: pre-existing, treatment induced and treatment boosted response. Pre-existing ADA was defined as ADA that were present in samples drawn during the pretreatment period (i.e., before the first isatuximab administration). Treatment-induced ADA was defined as ADA that developed at any time during the ADA on-study observation period in subjects without preexisting ADA, including subjects without pretreatment samples. Treatment boosted ADA was defined as pre-existing ADA that increased at least 2 titer steps between pre-treatment and post-treatment. Analysis was performed on ADA evaluable population which included subjects who received at least one dose of study drug from the IPd arm with at least one ADA assessment during the ADA on-study observation period with a reportable result.

End point type	Secondary

End point timeframe:

From randomisation up to 60 days after last dose of study drug (maximum duration 76.7 weeks)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for Pd arm.

End point values	IPd (Isatuximab + Pomalidomide + Dexamethasone)			
Subject group type	Reporting group			
Number of subjects analysed	151			
Units: subjects				
number (not applicable)				
Pre-existing ADA	0			
Treatment induced ADA	0			
Treatment boosted ADA	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organisation for Research and

Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20): Disease Symptoms Domain Score

End point title	Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20): Disease Symptoms Domain Score

End point description:

EORTC QLQ-MY20 is a validated questionnaire to assess the overall quality of life in subjects with multiple myeloma. Disease symptoms domain is one of the four domain scores. Disease symptoms domain score used 4-point scale (1 'Not at All' to 4 'Very Much'). Scores are averaged, and transformed to 0 -100 scale, where higher scores = more symptoms and lower health-related quality of life (HRQL) and lower score = less symptoms and more HRQL. Analysis was performed on safety population evaluable for disease symptoms. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (Cycle 3, Cycle 6, Cycle 9, and Cycle 17)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	137		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=130,135)	24.91 (± 20.67)	24.12 (± 20.54)		
Day 1: Cycle 3 (n=107,121)	-3.79 (± 16.09)	-2.07 (± 17.51)		
Day 1: Cycle 6 (n=68,101)	-4.08 (± 17.95)	-3.30 (± 16.01)		
Day 1: Cycle 9 (n=55,81)	-2.83 (± 15.04)	-4.66 (± 13.73)		
Day 1: Cycle 17 (n=10,13)	-3.33 (± 15.54)	0.00 (± 21.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20): Side Effects of Treatment Domain Score

End point title	Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20): Side Effects of Treatment Domain Score

End point description:

EORTC QLQ-MY20 is a validated questionnaire to assess the overall quality of life in subjects with multiple myeloma. Side effects of treatment domain is one of the four domain scores. Side effects of treatment domain score used 4-point scale (1 'Not at All' to 4 'Very Much'). Scores are averaged, and transformed to 0-100 scale, where higher scores = more side effects and lower HRQL and lower scores

= less side effects and better HRQL. Analysis was performed on safety population evaluable for side effects of treatment. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (Cycle 3, Cycle 6, Cycle 9, and Cycle 17)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	137		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=130,135)	17.49 (± 15.25)	15.60 (± 11.63)		
Day 1: Cycle 3 (n=107,121)	1.69 (± 11.54)	2.61 (± 13.39)		
Day 1: Cycle 6 (n=68,101)	-0.13 (± 15.10)	2.11 (± 11.78)		
Day 1: Cycle 9 (n=55,81)	1.43 (± 14.66)	3.14 (± 11.88)		
Day 1: Cycle 17 (n=10,13)	-2.93 (± 15.94)	3.02 (± 15.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life Working Group Health Status Measure 5 Dimensions (5D), 5 Levels (5L) (EQ-5D-5L) Score: Health State Utility Index Value

End point title	Change From Baseline in European Quality of Life Working Group Health Status Measure 5 Dimensions (5D), 5 Levels (5L) (EQ-5D-5L) Score: Health State Utility Index Value

End point description:

The EQ-5D-5L is a standardised measure of health status that provides a general assessment of health and wellbeing. The EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has a 5-level response: no problems, slight problems, moderate problems, severe problems, and extreme problems. Response options are measured with a 5-point Likert scale (for the 5L version). The 5D-5L systems are converted into a single index utility score between 0 to 1, where higher score indicates a better health state and lower score indicate worse health state. Analysis was performed on safety population evaluable for health state utility index. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (Cycle 3, Cycle 6, Cycle 9 and Cycle 17)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	140		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=134,138)	0.70 (± 0.24)	0.71 (± 0.21)		
Day 1: Cycle 3 (n=109,125)	-0.01 (± 0.22)	-0.01 (± 0.22)		
Day 1: Cycle 6 (n=69,101)	0.02 (± 0.22)	-0.00 (± 0.20)		
Day 1: Cycle 9 (n=55,82)	-0.03 (± 0.27)	-0.01 (± 0.15)		
Day 1: Cycle 17 (n=10,13)	-0.02 (± 0.19)	-0.01 (± 0.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life Working Group Health Status Measure 5 Dimensions, 5 Levels (EQ-5D-5L) Score: Visual Analogic Scale (VAS)

End point title	Change From Baseline in European Quality of Life Working Group Health Status Measure 5 Dimensions, 5 Levels (EQ-5D-5L) Score: Visual Analogic Scale (VAS)

End point description:

EQ-5D-5L is a standardised, subject-rated questionnaire to assess health-related quality of life. The EQ-5D-5L includes 2 components: the EQ-5D-5L health state utility index (descriptive system) and the EQ-5D-5L VAS. The VAS is designed to rate the subject's current health state on a scale from 0 to 100, where 0 represents the worst imaginable health state and 100 represents the best imaginable health state. Analysis was performed on safety population evaluable for visual analogue scale. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (Cycle 3, Cycle 6, Cycle 9, and Cycle 17)

End point values	Pd (Pomalidomide + Dexamethasone)	IPd (Isatuximab + Pomalidomide + Dexamethasone)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	140		
Units: centimeter				
arithmetic mean (standard deviation)				
Baseline (n=134,138)	65.38 (± 19.31)	66.62 (± 19.32)		
Day 1: Cycle 3 (n=109,125)	0.26 (± 17.37)	0.92 (± 19.41)		
Day 1: Cycle 6 (n=69,101)	2.49 (± 18.83)	1.19 (± 17.70)		
Day 1: Cycle 9 (n=55,82)	4.42 (± 19.78)	1.96 (± 16.60)		

Day 1: Cycle 17 (n=10,13)	-1.70 (± 12.39)	-3.00 (± 12.58)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE data was collected from the first dose up to 30 days following the last dose of study treatment; maximum duration up to 306.6 & 311.0 weeks for Pd and IPd arm, respectively. Per participant, deaths were collected to a maximum duration of 72.38 months.

Adverse event reporting additional description:

Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	IPd (isatuximab + pomalidomide + dexamethasone)

Reporting group description:

Participants received isatuximab 10 mg/kg IV infusion on Days 1, 8, 15, and 22 at Cycle 1, and then on Days 1 and 15 of subsequent cycles plus pomalidomide 4 mg PO on Days 1 to 21 of each 28-day treatment cycle and dexamethasone 40 mg (participants >= 75 years of age received 20 mg dexamethasone), PO or IV on Day 1, 8, 15, 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or participant's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 311.0 weeks).

Reporting group title	Pd (pomalidomide + dexamethasone)

Reporting group description:

Participants received pomalidomide 4 mg PO on Days 1 to 21 of each 28-day treatment cycle plus dexamethasone 40 mg (participants >= 75 years of age received 20 mg dexamethasone) PO on Days 1, 8, 15 and 22 of each 28-day treatment cycle until disease progression or unacceptable toxicity or participant's wish to discontinue study treatment, or any other reason, whichever comes first (maximum exposure: 306.6 weeks).

Serious adverse events	IPd (isatuximab + pomalidomide + dexamethasone)	Pd (pomalidomide + dexamethasone)	
Total subjects affected by serious adverse events			
subjects affected / exposed	112 / 152 (73.68%)	91 / 149 (61.07%)	
number of deaths (all causes)	109	113	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip Neoplasm Malignant Stage Unspecified			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Cell Carcinoma			

subjects affected / exposed	1 / 152 (0.66%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip Squamous Cell Carcinoma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	4 / 152 (2.63%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic Syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic Malignant Melanoma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tumour Associated Fever			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Hypotension			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Asthenia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease Progression			
subjects affected / exposed	9 / 152 (5.92%)	8 / 149 (5.37%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 7	0 / 4	
General Physical Health Deterioration			
subjects affected / exposed	1 / 152 (0.66%)	3 / 149 (2.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza Like Illness			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema Peripheral			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 152 (3.29%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	3 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral Swelling			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic Pain			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (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			
Chronic Obstructive Pulmonary Disease			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchopneumopathy			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	4 / 152 (2.63%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	3 / 152 (1.97%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Hypertension			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Oedema			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute Psychosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional State			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	3 / 152 (1.97%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Neck Fracture			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia Fracture			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spinal Compression Fracture			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion Related Reaction			
subjects affected / exposed	6 / 152 (3.95%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	6 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Complication			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Pectoris			
subjects affected / exposed	0 / 152 (0.00%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Unstable			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia Supraventricular			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis Coronary Artery			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	3 / 152 (1.97%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac Failure Chronic			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic Dysfunction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial Infarction			
subjects affected / exposed	3 / 152 (1.97%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Ganglia Infarction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed Level Of Consciousness			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebellar Infarction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cauda Equina Syndrome			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhage Intracranial			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intracranial Aneurysm			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Subdural Haematoma			

subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 152 (2.63%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vith Nerve Paresis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal Cord Paralysis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	10 / 152 (6.58%)	5 / 149 (3.36%)	
occurrences causally related to treatment / all	12 / 12	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	3 / 152 (1.97%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperviscosity Syndrome			
subjects affected / exposed	0 / 152 (0.00%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 152 (0.66%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	5 / 152 (3.29%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	3 / 5	2 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Splenic Infarction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (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	3 / 152 (1.97%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Detachment			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision Blurred			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis Ischaemic			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular Perforation			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Stone			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Failure			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus Ulcer			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic Foot			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	6 / 152 (3.95%)	6 / 149 (4.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hydronephrosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			
subjects affected / exposed	1 / 152 (0.66%)	3 / 149 (2.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Renal Aneurysm			

subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Impairment			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 152 (1.97%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Pain			
subjects affected / exposed	3 / 152 (1.97%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular Weakness			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis Of Jaw			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Necrosis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic Fracture			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (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	7 / 152 (4.61%)	4 / 149 (2.68%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical Pneumonia			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	7 / 152 (4.61%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	2 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	0 / 152 (0.00%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Covid-19 Pneumonia			
subjects affected / exposed	2 / 152 (1.32%)	3 / 149 (2.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Candida Pneumonia			

subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis Staphylococcal			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus Gastrointestinal Infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Sepsis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Enteroviral			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Sepsis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear, Nose And Throat Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster Disseminated			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	4 / 152 (2.63%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (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			
subjects affected / exposed	7 / 152 (4.61%)	3 / 149 (2.01%)	
occurrences causally related to treatment / all	1 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical Device Site Infection			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Meningitis Cryptococcal			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Listeria			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital Cellulitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis Jirovecii Pneumonia			
subjects affected / exposed	4 / 152 (2.63%)	5 / 149 (3.36%)	
occurrences causally related to treatment / all	2 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	35 / 152 (23.03%)	31 / 149 (20.81%)	
occurrences causally related to treatment / all	31 / 51	12 / 33	
deaths causally related to treatment / all	0 / 2	1 / 1	
Pneumonia Bacterial			
subjects affected / exposed	5 / 152 (3.29%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	3 / 6	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia Fungal			
subjects affected / exposed	1 / 152 (0.66%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Haemophilus			
subjects affected / exposed	2 / 152 (1.32%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Streptococcal			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Pneumococcal			
subjects affected / exposed	2 / 152 (1.32%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Influenzal			
subjects affected / exposed	2 / 152 (1.32%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia Viral			
subjects affected / exposed	3 / 152 (1.97%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis Acute			

subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 152 (0.66%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal Bacteraemia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			

subjects affected / exposed	1 / 152 (0.66%)	4 / 149 (2.68%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Sepsis			
subjects affected / exposed	4 / 152 (2.63%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 1	
Respiratory Tract Infection			
subjects affected / exposed	2 / 152 (1.32%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Bacteraemia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic Candida			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 152 (1.32%)	5 / 149 (3.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary Tract Infection			
subjects affected / exposed	7 / 152 (4.61%)	2 / 149 (1.34%)	
occurrences causally related to treatment / all	2 / 8	2 / 2	
deaths causally related to treatment / all	0 / 1	1 / 1	
Viral Upper Respiratory Tract Infection			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 152 (0.66%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	2 / 152 (1.32%)	3 / 149 (2.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	3 / 152 (1.97%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			

subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 152 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Disorder			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Lysis Syndrome			
subjects affected / exposed	1 / 152 (0.66%)	0 / 149 (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	IPd (isatuximab + pomalidomide + dexamethasone)	Pd (pomalidomide + dexamethasone)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 152 (95.39%)	139 / 149 (93.29%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 152 (7.24%)	7 / 149 (4.70%)	
occurrences (all)	17	9	
General disorders and administration site conditions			
Oedema Peripheral			
subjects affected / exposed	30 / 152 (19.74%)	18 / 149 (12.08%)	
occurrences (all)	38	22	
Fatigue			
subjects affected / exposed	30 / 152 (19.74%)	32 / 149 (21.48%)	
occurrences (all)	44	34	
Asthenia			

subjects affected / exposed	23 / 152 (15.13%)	29 / 149 (19.46%)	
occurrences (all)	37	36	
Pyrexia			
subjects affected / exposed	22 / 152 (14.47%)	19 / 149 (12.75%)	
occurrences (all)	27	21	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	12 / 152 (7.89%)	4 / 149 (2.68%)	
occurrences (all)	15	4	
Dyspnoea			
subjects affected / exposed	23 / 152 (15.13%)	13 / 149 (8.72%)	
occurrences (all)	33	14	
Cough			
subjects affected / exposed	14 / 152 (9.21%)	11 / 149 (7.38%)	
occurrences (all)	22	15	
Productive Cough			
subjects affected / exposed	8 / 152 (5.26%)	3 / 149 (2.01%)	
occurrences (all)	12	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	15 / 152 (9.87%)	14 / 149 (9.40%)	
occurrences (all)	17	17	
Investigations			
Weight Decreased			
subjects affected / exposed	10 / 152 (6.58%)	2 / 149 (1.34%)	
occurrences (all)	10	3	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 152 (7.24%)	9 / 149 (6.04%)	
occurrences (all)	15	11	
Infusion Related Reaction			
subjects affected / exposed	52 / 152 (34.21%)	1 / 149 (0.67%)	
occurrences (all)	56	1	
Cardiac disorders			
Atrial Fibrillation			

subjects affected / exposed	8 / 152 (5.26%)	2 / 149 (1.34%)	
occurrences (all)	11	2	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 152 (10.53%)	9 / 149 (6.04%)	
occurrences (all)	19	9	
Dizziness			
subjects affected / exposed	10 / 152 (6.58%)	5 / 149 (3.36%)	
occurrences (all)	11	5	
Peripheral Sensory Neuropathy			
subjects affected / exposed	18 / 152 (11.84%)	11 / 149 (7.38%)	
occurrences (all)	20	11	
Tremor			
subjects affected / exposed	13 / 152 (8.55%)	7 / 149 (4.70%)	
occurrences (all)	14	7	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	19 / 152 (12.50%)	17 / 149 (11.41%)	
occurrences (all)	27	19	
Neutropenia			
subjects affected / exposed	77 / 152 (50.66%)	52 / 149 (34.90%)	
occurrences (all)	192	96	
Febrile Neutropenia			
subjects affected / exposed	8 / 152 (5.26%)	0 / 149 (0.00%)	
occurrences (all)	10	0	
Eye disorders			
Cataract			
subjects affected / exposed	13 / 152 (8.55%)	11 / 149 (7.38%)	
occurrences (all)	14	11	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	8 / 152 (5.26%)	6 / 149 (4.03%)	
occurrences (all)	8	7	
Constipation			
subjects affected / exposed	27 / 152 (17.76%)	30 / 149 (20.13%)	
occurrences (all)	37	35	
Diarrhoea			

subjects affected / exposed	49 / 152 (32.24%)	32 / 149 (21.48%)	
occurrences (all)	86	44	
Nausea			
subjects affected / exposed	24 / 152 (15.79%)	14 / 149 (9.40%)	
occurrences (all)	27	14	
Stomatitis			
subjects affected / exposed	10 / 152 (6.58%)	4 / 149 (2.68%)	
occurrences (all)	14	4	
Vomiting			
subjects affected / exposed	20 / 152 (13.16%)	6 / 149 (4.03%)	
occurrences (all)	22	6	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	9 / 152 (5.92%)	11 / 149 (7.38%)	
occurrences (all)	9	12	
Rash			
subjects affected / exposed	11 / 152 (7.24%)	8 / 149 (5.37%)	
occurrences (all)	12	8	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	29 / 152 (19.08%)	24 / 149 (16.11%)	
occurrences (all)	32	25	
Arthralgia			
subjects affected / exposed	19 / 152 (12.50%)	18 / 149 (12.08%)	
occurrences (all)	22	18	
Bone Pain			
subjects affected / exposed	11 / 152 (7.24%)	13 / 149 (8.72%)	
occurrences (all)	13	14	
Muscle Spasms			
subjects affected / exposed	18 / 152 (11.84%)	17 / 149 (11.41%)	
occurrences (all)	19	20	
Muscular Weakness			
subjects affected / exposed	13 / 152 (8.55%)	8 / 149 (5.37%)	
occurrences (all)	14	8	
Musculoskeletal Chest Pain			

subjects affected / exposed	15 / 152 (9.87%)	7 / 149 (4.70%)	
occurrences (all)	16	7	
Myalgia			
subjects affected / exposed	12 / 152 (7.89%)	5 / 149 (3.36%)	
occurrences (all)	14	5	
Pain In Extremity			
subjects affected / exposed	12 / 152 (7.89%)	5 / 149 (3.36%)	
occurrences (all)	12	6	
Infections and infestations			
Bronchitis			
subjects affected / exposed	37 / 152 (24.34%)	16 / 149 (10.74%)	
occurrences (all)	65	29	
Influenza			
subjects affected / exposed	8 / 152 (5.26%)	6 / 149 (4.03%)	
occurrences (all)	9	7	
Nasopharyngitis			
subjects affected / exposed	23 / 152 (15.13%)	10 / 149 (6.71%)	
occurrences (all)	44	13	
Oral Herpes			
subjects affected / exposed	9 / 152 (5.92%)	3 / 149 (2.01%)	
occurrences (all)	18	3	
Pneumonia			
subjects affected / exposed	18 / 152 (11.84%)	10 / 149 (6.71%)	
occurrences (all)	29	10	
Upper Respiratory Tract Infection			
subjects affected / exposed	53 / 152 (34.87%)	28 / 149 (18.79%)	
occurrences (all)	121	51	
Urinary Tract Infection			
subjects affected / exposed	15 / 152 (9.87%)	13 / 149 (8.72%)	
occurrences (all)	21	15	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	17 / 152 (11.18%)	8 / 149 (5.37%)	
occurrences (all)	23	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2016	Study was given a name: ICARIA-MM; ECG assessments added at Cycle 2 Day 1 (pre-dose) and at end of treatment; fasting requirement prior to pomalidomide administration removed; specified 2 options for assessment of bone disease: skeletal survey and low-dose wholebody CT scan; specified subjects excluded due to amyloidosis included those with evidence of end organ damage or receiving treatment for amyloidosis; clarified that prior treatment with lenalidomide and a proteasome inhibitor could be alone or in combination; clarified that dexamethasone was not permitted within 14 days of study entry; clarified that after Cycle 1 Day 1, FLC was analysed by central laboratory only to confirm and document CR; modified text for analysis cytogenetic abnormalities to include others that may be identified from emerging data; IMWG criteria were updated to most recent guidance; removed PK sampling on Day 15 after Cycle 4; for subjects who discontinued due to PD, PRO assessments were added at end of therapy and 60 days post-treatment instead of every 30 days; subjects who discontinued without PD were to continue in the follow-up even if they initiated other anti-myeloma treatment; second primary malignancy was added as an adverse event of special interest (AESI); specified the treatments considered equivalent to ranitidine and diphenhydramine to prevent IRs; definition of renal dysfunction was updated from a creatinine clearance of <45 mL/min to <30 mL/min; guidance on resumption of treatment after Grade 2 Infusion reactions was updated; pomalidomide was not to be provided through POMALYST REMS program; procedures for subjects still on treatment at the PFS cut-off date were added; updated definitions for treatment exposure variables; PFS, OS, and DOR censoring text was harmonised; added women of childbearing potential should wear gloves when touching pomalidomide capsules or bottles; added possibility to modify ADA sampling based on updated information on isatuximab immunogenicity.
18 May 2017	Added changes from Amendment 2 (UK only); exclusion criterion 3 modified; screening window for women of childrearing potential extended to 28 days; pregnancy testing requirements were clarified to be consistent across documents with Pomalidomide Pregnancy Prevention Plan; antibody screening test was added after 4 infusions of isatuximab or anytime red blood cell transfusion was needed; clarified that Day 1 laboratory assessments and physical examinations could be performed the day before first treatment administration; IRC no longer needed to assess subjects for extramedullary disease at baseline to determine whether they required radiologic follow-up; added the missing benefit/risk assessment in protocol rationale section; added that subjects who did not have IRs with first 4 administrations of isatuximab could have premedication requirement reconsidered at Investigator's discretion; if subject could not tolerate dexamethasone during study treatment, methylprednisolone 100mg IV could have been administered as premedication only; clarified wording for dose reductions and cycle delay; clarified how to determine maximum interval for resumption of isatuximab administration following dosing interruption; clarified subject management and pregnancy testing for subjects still receiving treatment at the OS cut-off date; added instructions for overdose of non-investigational medicinal product; number of OS events to be observed before interim analysis was updated;ECOG PS was updated with most recent version and new reference was added; clarifications and edits to IMWG response criteria; added guidance for notification of early trial termination; clarified concentration of dexamethasone solution; Added that subjects would be followed for second primary malignancies during the follow-up; Specified that all IRs would be collected, but only IRs Grade >=3 were considered AESIs; Clarification of Investigator decision to continue study treatment based on local laboratory results.

25 October 2018	Clarified in Schedule of Assessments that minimal residual disease assessment to be performed in case of CR at end of treatment EOT, i.e. 30 days after last study treatment administration and post treatment follow-up period, i.e. 60±5 days and every 3 month (±7 days) after last study treatment administration; clarified Day 1 time window was ±2 days to allow time for reporting in the electronic case report form; the following additional guidance on neutropenia monitoring was added. If Grade 4 neutropenia, assess absolute neutrophil count every 2-3 days until ANC >=0.5 x 10^9/L and at least weekly thereafter until ANC >=1.0 x 10^9/L; clarified full dose of study treatment was to be maintained as planned within cycle for Grade 4 thrombocytopenia events; added description about precautions and consideration of risk-benefit ratio while using dexamethasone with CYP3A inhibitors; added details about various body parts (skull, spine, all long bones, pelvis, and chest) to be assessed during skeletal survey, for clarity; clarified contraception details for FCBP and partner on Day 1 and thromboprophylaxis; clarified that when there was a negative result for urine M-protein at Screening and Cycle 1 Day 1 then a repeat assessment should be performed at every 3 cycles (Cycle 4, Cycle 7, Cycle 10, etc); added details of bone marrow aspirate or biopsy as a parameter for MRD assessment; added second primary malignancies in the table of AESI category for consistency with the protocol body.
11 June 2019	Monthly pregnancy test for women of childbearing potential and contraception duration for men and women changed from 3 to 5 months after last isatuximab administration.
21 April 2020	An additional interim analysis on OS was performed when approximately 90% of events occurred; Typos were corrected.
26 November 2020	Additional hepatitis viral serology if HBV status unknown before treatment start, to be repeated if clinically indicated; description of study treatment discontinuation and restart procedure in case of viral reactivation; description of monitoring of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in case of viral reactivation; Infusion rate of isatuximab was revised; Dextrose 5% can also be used for isatuximab dilution; Removal of anti-drug antibodies tests after final analysis cut-off date leading to shortening of follow-up period to 30 days after last study treatment use for patients still on treatment at the time of amended protocol 07; Hospitalisation and exams report for SAEs will not be systematically requested; Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSARs) according to local regulatory requirements and Sponsor policy and forwarded to Investigators as necessary; Contingency measures to apply during a regional or national emergency declared by a governmental agency were described; Additional PFS analysis in Japanese subjects was cancelled; Use of ranitidine or equivalent as premedication was left to medical judgement; Location of monitoring details was added; minor formatting, typo corrections, and consistency changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32586908

http://www.ncbi.nlm.nih.gov/pubmed/33839618

http://www.ncbi.nlm.nih.gov/pubmed/34800109

http://www.ncbi.nlm.nih.gov/pubmed/35641409

http://www.ncbi.nlm.nih.gov/pubmed/35151415

http://www.ncbi.nlm.nih.gov/pubmed/31735560