



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 | v3 |
| This version publication date | 13 November 2024 |
| First version publication date | 17 April 2020 |
| Version creation reason | |

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 | Australia: 18 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | Japan: 13 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 9 |
| Country: Number of subjects enrolled | New Zealand: 13 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| 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 | United Kingdom: 5 |
| Country: Number of subjects enrolled | Russian Federation: 13 |
| Country: Number of subjects enrolled | Türkiye: 36 |
| 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 [\geq] 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 \geq 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 \geq 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 \geq 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 \geq 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 \geq 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 standard deviation | 65.2 \pm 9.5 | 66.6 \pm 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)

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|---|---------------------------------|
| 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 $\geq 25\%$ from lowest confirmed value in serum M protein (absolute increase must be $\geq 0.5\text{g/dL}$ or $\geq 1\text{g/dL}$ if lowest M component was $\geq 5\text{g/dL}$) or urine M-protein (absolute increase must be $\geq 200\text{mg/24hour}$), appearance of new lesion(s), $\geq 50\%$ increase from nadir in sum of the products of the maximal perpendicular diameters of measured lesions (SPD), or $\geq 50\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|----------------------------------|--|---|--|--|
| 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)

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|---|---|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|-------------------------------|--|---|--|--|
| 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

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|-----------------|---|
| 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.

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|----------------|-----------|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|-------------------------------|--|---|--|--|
| 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 $\geq 90\%$ reduction in serum M-protein plus urine M-protein level < 100 mg/24 h or $\geq 90\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|-------------------------------|--|---|--|--|
| 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 $\geq 25\%$ but $\leq 49\%$ 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, $\geq 50\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|-------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|----------------------------------|--|---|--|--|
| 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 $\geq 25\%$ 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 ≥ 1 g/dL if lowest M component was ≥ 5 g/dL; urine M-component (absolute increase must be ≥ 200 mg/24hour), appearance of new lesion(s), $\geq 50\%$ increase from nadir in SPD of >1 lesion, or $\geq 50\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|----------------------------------|--|---|--|--|
| 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: 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 $\geq 50\%$ reduction of serum M-protein and reduction in 24 hours urinary M-protein by $\geq 90\%$ or to < 200 mg/24 h. In addition to the above listed criteria, if present at baseline, a $\geq 50\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|----------------------------------|--|---|--|--|
| 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: 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 $\geq 25\%$ from lowest confirmed value in serum M-protein (absolute increase must be ≥ 0.5 g/dL), serum M-protein increase ≥ 1 g/dL if lowest M component was ≥ 5 g/dL; urine M-component (absolute increase must be

$\geq 200\text{mg}/24\text{h}$), appearance of new lesion(s), $\geq 50\%$ increase from nadir in SPD of >1 lesion, or $\geq 50\%$ increase in the longest diameter of a previous lesion >1 cm in short axis. PR: $\geq 50\%$ reduction of serum M-protein and reduction in 24h urinary M-protein by $\geq 90\%$ / $<200\text{mg}/24\text{h}$. 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 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 $\geq 50\%$ reduction of serum M-protein and reduction in 24 hours urinary M-protein by $\geq 90\%$ or to <200 mg/24 h. In addition to the above listed criteria, if present at baseline, a $\geq 50\%$ 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|----------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|-----------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|---|--|---|--|--|
| 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 + Dexamethason e) | | | |
| 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 (\pm 34.528) | | | |
| End of infusion: C1D15 (n=120) | 269.20 (\pm 32.622) | | | |
| End of infusion: C2D1 (n=134) | 299.85 (\pm 35.921) | | | |
| End of infusion: C4D1 (n=117) | 279.31 (\pm 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 + Dexamethason e) | | | |
| 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 (\pm 170.9185) | | | |
| C4D1 versus C1D1 (n=112) | 1.777 (\pm 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 + Dexamethason e) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 149 | | | |
| Units: mcg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| C1D1 (n=140) | 171.55 (\pm 38.299) | | | |
| C4D1 (n=114) | 294.96 (\pm 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 + Dexamethason e) | | | |
|--|---|--|--|--|
| 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 (C_{trough})

| | |
|-----------------|---|
| End point title | PK Parameter: Accumulation Ratio of Isatuximab at Trough Concentration (C _{trough}) ^[14] |
|-----------------|---|

End point description:

Accumulation Ratio was defined as the ratio of C_{trough} of Cycle 2 Day 1 versus Cycle 1 Day 8 and Cycle 4 Day 1 versus Cycle 1 Day 8, where C_{trough} 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 + Dexamethason e) | | | |
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
| 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 + Dexamethason e) | | | |
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|--------------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|--------------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|--------------------------------------|--|---|--|--|
| 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 + Dexamethason e) | IPd (Isatuximab + Pomalidomide + Dexamethason e) | | |
|--------------------------------------|--|---|--|--|
| 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. Deaths were collected from Day 1 up to end of study, approximately 84 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 \geq 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 \geq 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 occurrences (all) | 23 / 152 (15.13%) 37 | 29 / 149 (19.46%) 36 | |
| Pyrexia subjects affected / exposed occurrences (all) | 22 / 152 (14.47%) 27 | 19 / 149 (12.75%) 21 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 12 / 152 (7.89%) 15 | 4 / 149 (2.68%) 4 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 23 / 152 (15.13%) 33 | 13 / 149 (8.72%) 14 | |
| Cough subjects affected / exposed occurrences (all) | 14 / 152 (9.21%) 22 | 11 / 149 (7.38%) 15 | |
| Productive Cough subjects affected / exposed occurrences (all) | 8 / 152 (5.26%) 12 | 3 / 149 (2.01%) 3 | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 15 / 152 (9.87%) 17 | 14 / 149 (9.40%) 17 | |
| Investigations | | | |
| Weight Decreased subjects affected / exposed occurrences (all) | 10 / 152 (6.58%) 10 | 2 / 149 (1.34%) 3 | |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 11 / 152 (7.24%) 15 | 9 / 149 (6.04%) 11 | |
| Infusion Related Reaction subjects affected / exposed occurrences (all) | 52 / 152 (34.21%) 56 | 1 / 149 (0.67%) 1 | |
| Cardiac disorders | | | |
| Atrial Fibrillation | | | |

| | | | |
|--|-----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 8 / 152 (5.26%) 11 | 2 / 149 (1.34%) 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 occurrences (all) | 49 / 152 (32.24%) 86 | 32 / 149 (21.48%) 44 | |
| Nausea subjects affected / exposed occurrences (all) | 24 / 152 (15.79%) 27 | 14 / 149 (9.40%) 14 | |
| Stomatitis subjects affected / exposed occurrences (all) | 10 / 152 (6.58%) 14 | 4 / 149 (2.68%) 4 | |
| Vomiting subjects affected / exposed occurrences (all) | 20 / 152 (13.16%) 22 | 6 / 149 (4.03%) 6 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 9 / 152 (5.92%) 9 | 11 / 149 (7.38%) 12 | |
| Rash subjects affected / exposed occurrences (all) | 11 / 152 (7.24%) 12 | 8 / 149 (5.37%) 8 | |
| Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all) | 29 / 152 (19.08%) 32 | 24 / 149 (16.11%) 25 | |
| Arthralgia subjects affected / exposed occurrences (all) | 19 / 152 (12.50%) 22 | 18 / 149 (12.08%) 18 | |
| Bone Pain subjects affected / exposed occurrences (all) | 11 / 152 (7.24%) 13 | 13 / 149 (8.72%) 14 | |
| Muscle Spasms subjects affected / exposed occurrences (all) | 18 / 152 (11.84%) 19 | 17 / 149 (11.41%) 20 | |
| Muscular Weakness subjects affected / exposed occurrences (all) | 13 / 152 (8.55%) 14 | 8 / 149 (5.37%) 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 | <p>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.</p> |
| 18 May 2017 | <p>Added changes from Amendment 2 (UK only); exclusion criterion 3 modified; screening window for women of childbearing 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.</p> |

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|------------------|---|
| 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 $\geq 0.5 \times 10^9/L$ and at least weekly thereafter until ANC $\geq 1.0 \times 10^9/L$; 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>