



Clinical trial results:

A Phase 3 Randomized, Multicenter Study of Subcutaneous versus Intravenous Administration of Daratumumab in Subjects with Relapsed or Refractory Multiple Myeloma

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2017-000206-38 |
| Trial protocol | SE CZ GB GR ES FR PL IT |
| Global end of trial date | 04 September 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 18 November 2023 |
| First version publication date | 18 November 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | 54767414MMY3012 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03277105 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route 202 South, Raritan, New Jersey, United States, 08869 |
| Public contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 September 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to show that subcutaneous (SC) administration of daratumumab co-formulated with recombinant human hyaluronidase PH20 (Dara SC) was non-inferior to intravenous (IV) administration of daratumumab (Dara IV) in terms of the overall response rate (ORR) and maximum trough concentration (C_{trough}).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 31 October 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 28 |
| Country: Number of subjects enrolled | Brazil: 25 |
| Country: Number of subjects enrolled | Canada: 36 |
| Country: Number of subjects enrolled | Czechia: 36 |
| Country: Number of subjects enrolled | Spain: 26 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | United Kingdom: 33 |
| Country: Number of subjects enrolled | Greece: 7 |
| Country: Number of subjects enrolled | Israel: 13 |
| Country: Number of subjects enrolled | Italy: 26 |
| Country: Number of subjects enrolled | Japan: 42 |
| Country: Number of subjects enrolled | Korea, Republic of: 11 |
| Country: Number of subjects enrolled | Poland: 65 |
| Country: Number of subjects enrolled | Russian Federation: 55 |
| Country: Number of subjects enrolled | Sweden: 36 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | Ukraine: 47 |
| Country: Number of subjects enrolled | United States: 6 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 522 |
| EEA total number of subjects | 212 |

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) | 221 |
| From 65 to 84 years | 293 |
| 85 years and over | 8 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 522 subjects were enrolled, of which 518 subjects were treated and none of the subject completed the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Daratumumab IV |

Arm description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Daratumumab |
| Investigational medicinal product code | |
| Other name | JNJ-54767414 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Daratumumab 16 milligrams per kilogram (mg/kg) was administered once weekly in Cycles 1 and 2, every 2 weeks in Cycles 3 to 6, and every 4 weeks thereafter until disease progression, unacceptable toxicity or the end of study.

| | |
|------------------|----------------|
| Arm title | Daratumumab SC |
|------------------|----------------|

Arm description:

Subjects received daratumumab 1800 mg subcutaneous (SC) injection co-formulated with recombinant human hyaluronidase (rHuPH20) 2000 Units per millilitre (U/mL), once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Daratumumab |
| Investigational medicinal product code | |
| Other name | JNJ-54767414 |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received a fixed dose of daratumumab 1800 mg with rHuPH20 2000 U/mL, once weekly in Cycle 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks in Cycle 7 and thereafter until disease progression, unacceptable toxicity or the end of study.

| Number of subjects in period 1 | Daratumumab IV | Daratumumab SC |
|---------------------------------------|----------------|----------------|
| Started | 259 | 263 |
| Treated (Safety Analysis Set) | 258 | 260 |
| Completed | 0 | 0 |
| Not completed | 259 | 263 |
| Adverse event, serious fatal | 129 | 124 |
| Consent withdrawn by subject | 10 | 10 |
| Unspecified | 118 | 125 |
| Lost to follow-up | 2 | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Daratumumab IV |
|-----------------------|----------------|

Reporting group description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| | |
|-----------------------|----------------|
| Reporting group title | Daratumumab SC |
|-----------------------|----------------|

Reporting group description:

Subjects received daratumumab 1800 mg subcutaneous (SC) injection co-formulated with recombinant human hyaluronidase (rHuPH20) 2000 Units per millilitre (U/mL), once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| Reporting group values | Daratumumab IV | Daratumumab SC | Total |
|---|----------------|----------------|-------|
| Number of subjects | 259 | 263 | 522 |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 100 | 121 | 221 |
| From 65-84 years | 151 | 142 | 293 |
| 85 years and over | 8 | 0 | 8 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 66.8 | 65.3 | - |
| standard deviation | ± 10.16 | ± 9.11 | - |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 110 | 127 | 237 |
| Male | 149 | 136 | 285 |
| Stage of Disease (ISS) | | | |
| Units: Subjects | | | |
| Stage I | 94 | 82 | 176 |
| Stage II | 89 | 101 | 190 |
| Stage III | 76 | 79 | 155 |
| Not reported | 0 | 1 | 1 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | 1 |
| Asian | 40 | 32 | 72 |
| Black or African American | 5 | 9 | 14 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 1 |
| White | 201 | 207 | 408 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 12 | 14 | 26 |
| Ethnicity (NIH/OMB) | | | |

| | | | |
|------------------------------------|---------|--------|-----|
| Units: Subjects | | | |
| Hispanic or Latino | 9 | 14 | 23 |
| Not Hispanic or Latino | 227 | 225 | 452 |
| Unknown or Not Reported | 23 | 24 | 47 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| AUSTRALIA | 15 | 13 | 28 |
| BRAZIL | 10 | 15 | 25 |
| CANADA | 16 | 20 | 36 |
| CZECH REPUBLIC | 20 | 16 | 36 |
| FRANCE | 6 | 10 | 16 |
| GREECE | 1 | 6 | 7 |
| ISRAEL | 5 | 8 | 13 |
| ITALY | 10 | 16 | 26 |
| JAPAN | 24 | 18 | 42 |
| POLAND | 39 | 26 | 65 |
| RUSSIAN FEDERATION | 28 | 27 | 55 |
| SOUTH KOREA | 7 | 4 | 11 |
| SPAIN | 14 | 12 | 26 |
| SWEDEN | 18 | 18 | 36 |
| TAIWAN | 6 | 8 | 14 |
| UKRAINE | 22 | 25 | 47 |
| UNITED KINGDOM | 16 | 17 | 33 |
| UNITED STATES | 2 | 4 | 6 |
| Number of prior lines | | | |
| Units: Subjects | | | |
| Less than or equal to (<= 4) Lines | 175 | 174 | 349 |
| Greater than (>) 4 Lines | 84 | 89 | 173 |
| Refractory status | | | |
| Units: Subjects | | | |
| Both PI and IMiD | 133 | 125 | 258 |
| IMiD only | 81 | 67 | 148 |
| None | 26 | 41 | 67 |
| PI only | 19 | 30 | 49 |
| Weight group | | | |
| Units: Subjects | | | |
| <=65 | 92 | 94 | 186 |
| >65 - 85 | 105 | 102 | 207 |
| >85 | 61 | 66 | 127 |
| Not Weighed | 1 | 1 | 2 |
| AgeContinuous | | | |
| Units: years | | | |
| arithmetic mean | 66.8 | 65.3 | |
| standard deviation | ± 10.16 | ± 9.11 | - |

End points

End points reporting groups

| | |
|--|----------------|
| Reporting group title | Daratumumab IV |
| Reporting group description: Subjects received daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days. | |
| Reporting group title | Daratumumab SC |
| Reporting group description: Subjects received daratumumab 1800 mg subcutaneous (SC) injection co-formulated with recombinant human hyaluronidase (rHuPH20) 2000 Units per millilitre (U/mL), once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days. | |

Primary: Maximum Trough Concentration (Ctough) of Daratumumab

| | |
|--|---|
| End point title | Maximum Trough Concentration (Ctough) of Daratumumab ^[1] |
| End point description: Maximum Ctough was defined as the serum predose concentration of daratumumab on Cycle 3 Day 1. Pharmacokinetics-evaluable analysis set included subjects who received all 8 weekly full doses of daratumumab IV or daratumumab SC in Cycle 1 and Cycle 2 and provided a pre-dose pharmacokinetic sample on Cycle 3 Day 1 within the sampling window of 8 hours prior to the start of dose administration. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: Predose on Cycle 3 Day 1 (each cycle of 28 days) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

| End point values | Daratumumab IV | Daratumumab SC | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 149 | | |
| Units: micrograms per millilitre (mcg/mL) | | | | |
| arithmetic mean (standard deviation) | 496 (± 231) | 581 (± 315) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR)

| | |
|---|--|
| End point title | Overall Response Rate (ORR) ^[2] |
| End point description: ORR was defined as the percentage of subjects who achieved partial response (PR) or better according to International Myeloma Working Group (IMWG) criteria, during or after study treatment. IMWG criteria | |

for PR: greater than or equal to (\geq) 50 percent (%) reduction of serum M-protein and reduction in 24-hour urinary M-protein by \geq 90% or to less than ($<$) 200 milligrams (mg)/24 hours. Intent-to-treat (ITT) analysis set included subjects randomised into the study.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Up to 3 years | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 39.8 (33.8 to 46.0) | 43.7 (37.6 to 50.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment-emergent Infusion-related Reactions (IRR)

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Treatment-emergent Infusion-related Reactions (IRR) |
|-----------------|---|

End point description:

Percentage of subjects with treatment-emergent infusion-related reactions were reported. Safety analysis set included all randomised subjects who receive at least 1 dose of study drug and were analysed according to the actual treatment that they received.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 3 years

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 258 | 260 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 34.5 (28.7 to 40.6) | 12.7 (8.9 to 17.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Very Good Partial Response (VGPR) or Better

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Very Good Partial Response (VGPR) or Better |
|-----------------|---|

End point description:

VGPR or better was defined as the percentage of subjects who achieved VGPR or better (VGPR, complete response (CR) or stringent complete response [sCR]), based on computerized algorithm as per IMWG criteria during or after the study treatment. IMWG criteria for VGPR: Serum and urine M-component detectable by immunofixation but not on electrophoresis, or ≥ 90 percent (%) reduction in serum M-protein plus urine M-protein < 100 milligrams (mg)/24 hours, CR: Negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas and $< 5\%$ plasma cells (PCs) in bone marrow. sCR: CR plus normal FLC ratio, and absence of clonal PCs by immunohistochemistry (IHC), immunofluorescence or 2 to 4 color flow cytometry. ITT analysis set included subjects randomised into the study

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 3 years

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 21.6 (16.8 to 27.1) | 23.6 (18.6 to 29.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

| | |
|-----------------|---------------------------------|
| End point title | Progression Free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS was defined as time from date of randomisation to either progression of disease (PD), death due to any cause, whichever occurs first. IMWG criteria for PD: Increase of 25% from lowest response value in Serum M component (absolute increase [AI] must be ≥ 0.5 grams per decilitre (g/dL), Urine M-component (AI must be ≥ 200 mg/24 hours), Subjects without measurable serum and urine M-protein levels: difference between involved and uninvolved free light chain (FLC) levels (AI must be > 10 milligrams per decilitre (mg/dL), subjects without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow PC% (absolute percentage must be $\geq 10\%$), definite development of new bone lesions or soft tissue plasmacytomas or increase in size of bone lesions or tissue plasmacytomas and development of hypercalcemia (serum calcium > 11.5 mg/dL) that can be attributed solely to PC proliferative disorder. ITT analysis set included subjects randomised into the study.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 3 years

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 6.08 (4.73 to 7.43) | 5.62 (4.70 to 7.49) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Complete Response (Including sCR) or Better

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Complete Response (Including sCR) or Better |
|-----------------|---|

End point description:

CR or better was defined as percentage of subjects with a CR or better (CR or stringent complete response [sCR]) based on computerized algorithm as per IMWG criteria. IMWG criteria for CR- negative immunofixation on the serum and urine, and disappearance of any soft tissue plasmacytomas, and <5% PCs in bone marrow. sCR: CR plus normal FLC ratio, and absence of clonal PCs by IHC, immunofluorescence or 2- to 4 color flow cytometry. ITT analysis set included subjects randomised into the study.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 3 years

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 5.4 (3.0 to 8.9) | 4.6 (2.4 to 7.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Therapy

| | |
|-----------------|----------------------|
| End point title | Time to Next Therapy |
|-----------------|----------------------|

End point description:

Time to next therapy was defined as the time from randomisation to the start of the first subsequent anti-cancer therapy. ITT analysis set included subjects randomised into the study.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 3 years

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 9.43 (8.15 to 10.71) | 8.80 (7.59 to 10.91) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

| | |
|--|-----------------------|
| End point title | Overall Survival (OS) |
| End point description: | |
| OS was defined as the time from the date of randomisation to the date of the subject's death due to any cause. ITT analysis set included subjects randomised into the study. Here, 99999 signifies lower limit of 95% CI were not estimable due to lower number of events. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 3 years | |

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 | 263 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 25.56 (22.05 to 99999) | 28.19 (22.77 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Patient-Reported Satisfaction With Therapy as Assessed with Cancer Therapy Satisfaction Questionnaire (CTSQ) at Specified Timepoints

| | |
|--|--|
| End point title | Patient-Reported Satisfaction With Therapy as Assessed with Cancer Therapy Satisfaction Questionnaire (CTSQ) at Specified Timepoints |
| End point description: | |
| Modified-CTSQ contain 9 items (2 items for Thoughts about Cancer Therapy and 7 items in a defined domain of Satisfaction with Therapy) specific to satisfaction with therapy and for comparison of SC and IV administration. Satisfaction with therapy was calculated based on 7-items using 5-point verbal rating | |

scale, where 1= never and 5= always. Scores were averaged and transformed to a 0-100 scale; higher scores represent better health. At least 5 of the 7 items within the Satisfaction with Therapy domain had to be completed to calculate a domain score. No domain score was calculated for Thoughts about Cancer Therapy. ITT analysis set included subjects randomised into the study. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint and 'n' (number of subjects analysed) signifies the number of subjects analysed at a specified time point.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 (Days 8,15 and 22), Cycle 2 (Days 1,8,15 and 22), Cycle 3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21 and 22 (Day 1)

| End point values | Daratumumab IV | Daratumumab SC | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 239 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 8 (n=227,230) | 70.5 (± 15.98) | 76.9 (± 14.64) | | |
| Cycle 1 Day 15 (n=226,238) | 72.1 (± 16.72) | 78.8 (± 14.94) | | |
| Cycle 1 Day 22 (n=226,239) | 72.8 (± 16.20) | 78.7 (± 15.75) | | |
| Cycle 2 Day 1 (n=239,238) | 74.2 (± 16.44) | 79.7 (± 16.58) | | |
| Cycle 2 Day 8 (n=227,232) | 74.8 (± 15.57) | 80.1 (± 17.24) | | |
| Cycle 2 Day 15 (n=228,224) | 74.3 (± 16.94) | 80.0 (± 17.37) | | |
| Cycle 2 Day 22 (n=221,214) | 75.2 (± 16.47) | 79.3 (± 18.65) | | |
| Cycle 3 Day 1 (n=217, 224) | 76.0 (± 17.39) | 80.4 (± 17.78) | | |
| Cycle 4 Day 1 (n=205,209) | 76.6 (± 17.22) | 79.5 (± 19.88) | | |
| Cycle 5 Day 1 (n=187,188) | 77.1 (± 17.11) | 79.6 (± 18.95) | | |
| Cycle 6 Day 1 (n=168,159) | 76.1 (± 17.79) | 81.9 (± 18.34) | | |
| Cycle 7 Day 1 (n=150,137) | 78.6 (± 16.01) | 85.0 (± 16.87) | | |
| Cycle 8 Day 1 (n=135,127) | 79.2 (± 15.54) | 85.0 (± 15.18) | | |
| Cycle 9 Day 1 (n=121,113) | 79.8 (± 15.27) | 85.2 (± 15.03) | | |
| Cycle 10 Day 1 (n=111,103) | 79.4 (± 14.73) | 85.8 (± 13.31) | | |
| Cycle 11 Day 1 (n=96,94) | 79.1 (± 15.55) | 84.8 (± 13.05) | | |
| Cycle 12 Day 1 (n=83, 81) | 80.3 (± 15.88) | 85.4 (± 14.70) | | |
| Cycle 13 Day 1 (n=77,76) | 79.6 (± 16.57) | 84.4 (± 15.09) | | |
| Cycle 14 Day 1 (n=60,61) | 80.6 (± 14.62) | 83.5 (± 15.54) | | |
| Cycle 15 Day 1 (n=44,40) | 80.2 (± 15.22) | 86.2 (± 13.51) | | |
| Cycle 16 Day 1 (n=29,29) | 79.4 (± 14.84) | 88.5 (± 13.10) | | |
| Cycle 17 Day 1 (n=15,20) | 79.0 (± 14.34) | 90.9 (± 11.26) | | |
| Cycle 18 Day 1 (n=8,10) | 84.8 (± 14.13) | 91.4 (± 11.57) | | |
| Cycle 19 Day 1 (n=2,8)) | 92.9 (± 10.10) | 89.3 (± 13.36) | | |
| Cycle 20 Day 1 (n=0,4) | 99999 (± 99999) | 86.6 (± 18.53) | | |
| Cycle 21 Day 1 (n=0,3) | 99999 (± 99999) | 84.5 (± 20.93) | | |
| Cycle 22 Day 1 (n=0,1) | 99999 (± 99999) | 96.4 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|--|----------------------|
| End point title | Duration of Response |
| End point description: Duration of response was defined as the duration from the date of initial documentation of a response (PR or better) to the date of first documented evidence of progressive disease according to the IMWG criteria. PD was defined as an increase of 25% from the lowest response value in one of the following: serum and urine M-component (AI must be $\geq 0.5\text{g/dL}$ and $\geq 200\text{mg/24 hours}$ respectively); Only in subjects without measurable serum and urine M-protein levels the difference between involved and uninvolved FLC levels (AI must be $>10\text{mg/dL}$); Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas; Development of hypercalcemia (corrected serum calcium $>11.5\text{mg/dL}$) that can be attributed solely to PC proliferative disorder. ITT analysis set included subjects randomised into the study. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: Up to 3 years | |

| End point values | Daratumumab IV | Daratumumab SC | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 103 | 115 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.64 (9.23 to 15.64) | 10.15 (9.23 to 13.77) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Partial Response (PR) or Better

| | |
|---|---|
| End point title | Time to Partial Response (PR) or Better |
| End point description: Time to PR or better was defined as the time from randomisation until onset of first response of PR or better. ITT analysis set included subjects randomised into the study. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. | |
| End point type | Secondary |
| End point timeframe: Up to 3 years | |

| End point values | Daratumumab IV | Daratumumab SC | | |
|-------------------------------|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 103 | 115 | | |
| Units: months | | | | |
| median (full range (min-max)) | 1.02 (0.9 to 24.8) | 1.02 (0.9 to 9.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Complete Response (CR) or Better

| | |
|------------------------|---|
| End point title | Time to Complete Response (CR) or Better |
| End point description: | Time to CR or better was defined as the time from randomisation until onset of first CR or better. ITT analysis set included subjects randomised into the study. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. |
| End point type | Secondary |
| End point timeframe: | Up to 3 years |

| End point values | Daratumumab IV | Daratumumab SC | | |
|-------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 12 | | |
| Units: months | | | | |
| median (full range (min-max)) | 7.23 (1.1 to 14.9) | 9.26 (1.2 to 23.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Very Good Partial Response (VGPR) or Better

| | |
|------------------------|---|
| End point title | Time to Very Good Partial Response (VGPR) or Better |
| End point description: | Time to VGPR or better was defined as the time from randomisation until onset of first VGPR or better. ITT analysis set included subjects randomised into the study. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint. |
| End point type | Secondary |
| End point timeframe: | Up to 3 years |

| End point values | Daratumumab IV | Daratumumab SC | | |
|-------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 62 | | |
| Units: months | | | | |
| median (full range (min-max)) | 1.92 (0.9 to 22.8) | 1.95 (1.0 to 19.4) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years

Adverse event reporting additional description:

Safety analysis set included as all randomised subjects who received at least 1 dose of study drug and were analysed according to the actual treatment that they received.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | Daratumumab 1800 mg SC Injection |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received daratumumab 1800 mg subcutaneous (SC) injection co-formulated with recombinant human hyaluronidase (rHuPH20) 2000 Unit per milliliter (U/mL), once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Daratumumab 16 mg/kg IV Infusion |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly in Cycles 1 and 2, every 2 weeks in Cycle 3 to 6, every 4 weeks thereafter until disease progression, unacceptable toxicity, withdrawal of consent, the investigator decides to stop treatment, or the start of subsequent anticancer therapy. The duration for each cycle was 28 days.

| Serious adverse events | Daratumumab 1800 mg SC Injection | Daratumumab 16 mg/kg IV Infusion | |
|---|----------------------------------|----------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 83 / 260 (31.92%) | 89 / 258 (34.50%) | |
| number of deaths (all causes) | 126 | 130 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Plasmacytoma | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate Cancer Recurrent | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to Liver | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Neoplasm Malignant | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Cancer | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon Cancer | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Adenocarcinoma of Colon | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal Squamous Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid Neoplasm | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour Associated Fever | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Circulatory Collapse | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| 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 | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 260 (1.54%) | 6 / 258 (2.33%) | |
| occurrences causally related to treatment / all | 3 / 4 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Performance Status Decreased | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple Organ Dysfunction Syndrome | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| General Physical Health Deterioration | | | |
| subjects affected / exposed | 4 / 260 (1.54%) | 6 / 258 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 3 | |
| Fatigue | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest Pain | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest Discomfort | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Pelvic Pain | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Obstructive Pulmonary Disease | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 2 / 260 (0.77%) | 0 / 258 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 |
| Respiratory Distress | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pulmonary Thrombosis | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pulmonary Oedema | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pulmonary Embolism | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Lung Disorder | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hypoxia | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Epistaxis | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (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 | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional State | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Oxygen Saturation Decreased | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General Physical Condition Abnormal | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood Pressure Increased | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral Neck Fracture | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur Fracture | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Upper Limb Fracture | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural Haematoma | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus Fracture | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Coronary Syndrome | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Pectoris | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular Block | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular Block Complete | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac Failure | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Atrial Fibrillation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial Ischaemia | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial Infarction | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac Failure Chronic | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiopulmonary Failure | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nervous system disorders | | | |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Cord Compression | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Sensory Neuropathy | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoparesis | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iiird Nerve Paralysis | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Insufficiency | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Infarction | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Brain Oedema | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Blood and lymphatic system disorders | | | |
| Hyperviscosity Syndrome | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile Neutropenia | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Disseminated Intravascular Coagulation | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 6 / 260 (2.31%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 0 / 7 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 260 (1.15%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 1 / 3 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deafness Neurosensory | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Ileus | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal Hernia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gingival Bleeding | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal Haemorrhage | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal Varices Haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small Intestinal Obstruction | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 4 / 260 (1.54%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myeloma Cast Nephropathy | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (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 | 3 / 260 (1.15%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myofascial Pain Syndrome | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular Weakness | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone Pain | | | |
| subjects affected / exposed | 5 / 260 (1.92%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back Pain | | | |
| subjects affected / exposed | 3 / 260 (1.15%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trismus | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Pain | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological Fracture | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in Extremity | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck Pain | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Acute Hepatitis B | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Infection | | | |
| subjects affected / exposed | 5 / 260 (1.92%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 6 / 7 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 3 / 260 (1.15%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Listeriosis | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 |
| Influenza | | |
| subjects affected / exposed | 3 / 260 (1.15%) | 2 / 258 (0.78%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Infection | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Hepatitis B Reactivation | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 |
| Furuncle | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Escherichia Infection | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Device Related Infection | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Corona Virus Infection | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 |
| Campylobacter Gastroenteritis | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastoiditis | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis Cryptococcal | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis Pneumococcal | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic Sepsis | | | |
| subjects affected / exposed | 1 / 260 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis Jirovecii Pneumonia | | | |

| | | |
|---|------------------|------------------|
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 |
| Pneumonia | | |
| subjects affected / exposed | 12 / 260 (4.62%) | 13 / 258 (5.04%) |
| occurrences causally related to treatment / all | 4 / 12 | 4 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 |
| Respiratory Syncytial Virus Bronchitis | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Respiratory Tract Infection | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 2 / 258 (0.78%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Rhinovirus Infection | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Sepsis | | |
| subjects affected / exposed | 4 / 260 (1.54%) | 4 / 258 (1.55%) |
| occurrences causally related to treatment / all | 1 / 5 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 2 / 2 |
| Septic Shock | | |
| subjects affected / exposed | 3 / 260 (1.15%) | 4 / 258 (1.55%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 3 |
| Staphylococcal Sepsis | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Upper Respiratory Tract Infection | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metabolism and nutrition disorders | | | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 260 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 260 (0.77%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |

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

| Non-serious adverse events | Daratumumab 1800 mg SC Injection | Daratumumab 16 mg/kg IV Infusion | |
|--|----------------------------------|----------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 217 / 260 (83.46%) | 216 / 258 (83.72%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 16 / 260 (6.15%) | 23 / 258 (8.91%) | |
| occurrences (all) | 22 | 33 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 15 / 260 (5.77%) | 25 / 258 (9.69%) | |
| occurrences (all) | 15 | 26 | |
| Dizziness | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 15 / 260 (5.77%) 20 | 11 / 258 (4.26%) 12 | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 49 / 260 (18.85%) | 50 / 258 (19.38%) | |
| occurrences (all) | 137 | 180 | |
| Neutropenia | | | |
| subjects affected / exposed | 52 / 260 (20.00%) | 34 / 258 (13.18%) | |
| occurrences (all) | 110 | 87 | |
| Lymphopenia | | | |
| subjects affected / exposed | 21 / 260 (8.08%) | 17 / 258 (6.59%) | |
| occurrences (all) | 34 | 31 | |
| Leukopenia | | | |
| subjects affected / exposed | 18 / 260 (6.92%) | 10 / 258 (3.88%) | |
| occurrences (all) | 35 | 20 | |
| Anaemia | | | |
| subjects affected / exposed | 71 / 260 (27.31%) | 64 / 258 (24.81%) | |
| occurrences (all) | 143 | 143 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 15 / 260 (5.77%) | 17 / 258 (6.59%) | |
| occurrences (all) | 20 | 21 | |
| Pyrexia | | | |
| subjects affected / exposed | 36 / 260 (13.85%) | 34 / 258 (13.18%) | |
| occurrences (all) | 56 | 48 | |
| Oedema Peripheral | | | |
| subjects affected / exposed | 10 / 260 (3.85%) | 15 / 258 (5.81%) | |
| occurrences (all) | 10 | 21 | |
| Fatigue | | | |
| subjects affected / exposed | 33 / 260 (12.69%) | 26 / 258 (10.08%) | |
| occurrences (all) | 43 | 29 | |
| Chills | | | |
| subjects affected / exposed | 15 / 260 (5.77%) | 32 / 258 (12.40%) | |
| occurrences (all) | 16 | 32 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| Constipation subjects affected / exposed occurrences (all) | 16 / 260 (6.15%) 17 | 22 / 258 (8.53%) 26 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 41 / 260 (15.77%) 64 | 32 / 258 (12.40%) 50 | |
| Nausea subjects affected / exposed occurrences (all) | 24 / 260 (9.23%) 29 | 31 / 258 (12.02%) 37 | |
| Vomiting subjects affected / exposed occurrences (all) | 16 / 260 (6.15%) 17 | 21 / 258 (8.14%) 24 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal Congestion subjects affected / exposed occurrences (all) | 10 / 260 (3.85%) 11 | 13 / 258 (5.04%) 13 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 15 / 260 (5.77%) 19 | 28 / 258 (10.85%) 34 | |
| Cough subjects affected / exposed occurrences (all) | 25 / 260 (9.62%) 39 | 36 / 258 (13.95%) 37 | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 14 / 260 (5.38%) 15 | 14 / 258 (5.43%) 15 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 33 / 260 (12.69%) 40 | 18 / 258 (6.98%) 20 | |
| Back Pain subjects affected / exposed occurrences (all) | 31 / 260 (11.92%) 48 | 36 / 258 (13.95%) 42 | |
| Bone Pain subjects affected / exposed occurrences (all) | 17 / 260 (6.54%) 17 | 10 / 258 (3.88%) 12 | |

| | | | |
|---|-------------------------|-------------------------|--|
| Musculoskeletal Chest Pain subjects affected / exposed occurrences (all) | 19 / 260 (7.31%) 27 | 16 / 258 (6.20%) 19 | |
| Musculoskeletal Pain subjects affected / exposed occurrences (all) | 15 / 260 (5.77%) 16 | 13 / 258 (5.04%) 16 | |
| Pain in Extremity subjects affected / exposed occurrences (all) | 19 / 260 (7.31%) 21 | 13 / 258 (5.04%) 17 | |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 14 / 260 (5.38%) 14 | 9 / 258 (3.49%) 9 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 28 / 260 (10.77%) 41 | 21 / 258 (8.14%) 30 | |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 44 / 260 (16.92%) 73 | 30 / 258 (11.63%) 41 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 13 / 260 (5.00%) 13 | 17 / 258 (6.59%) 22 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 07 December 2017 | The purpose of this amendment was to address feedback from regulatory health authorities including updating inclusion criteria for measurable disease and hepatitis B virus (HBV) status, to provide additional instruction in the event of infusion-related reactions, and to clarify methodology of local bone marrow testing. |
| 13 August 2018 | The purpose of this amendment was to made an update to the regulatory strategy, including an update to the statistical plan, is being implemented to allow Japan to enroll beyond the initially planned 480 subjects in order to meet a health authority commitment. Clarifications had also been made to ensure accuracy and clarity throughout the protocol. |
| 21 January 2020 | The purpose of this amendment was to define the end of the data collection period and to clarify access to drug treatment after data collection in the study electronic case report form (eCRF) had ended. |
| 01 April 2020 | The purpose of this amendment was to provide flexibility for study investigators to prioritize the safety of their patients during the global coronavirus (COVID-19) pandemic. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported