



Clinical trial results:

An Open-label, Multicenter, Phase 2 Trial Investigating the Efficacy and Safety of Daratumumab in Subjects With Multiple Myeloma Who Have Received at Least 3 Prior Lines of Therapy(Including a Proteasome Inhibitor and Immunomodulatory drug (IMiD)) or are Double Refractory to a Proteasome Inhibitor and an IMiD

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-000752-18 |
| Trial protocol | BE ES |
| Global end of trial date | 30 May 2017 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 02 June 2018 |
| First version publication date | 02 June 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | CR102651 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01985126 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route 202, Raritan, United States, NJ 08869 |
| Public contact | Clinical Registry Group, Janssen Research and Development LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Research and 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 | 30 May 2017 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to determine the efficacy of 2 daratumumab treatment regimens, as measured by the overall response rate (ORR) (partial response [PR] or better), in subjects with multiple myeloma who had received at least 3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD) or whose disease was double refractory to both a PI and an IMiD agent.

Protection of trial subjects:

The 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 Practices and applicable regulatory requirements. The safety assessments included clinical laboratory tests (hematology and serum chemistry), vital sign measurements, electrocardiograms (ECGs), physical examinations and adverse events were reported throughout the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 30 September 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 44 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 22 |
| Country: Number of subjects enrolled | Spain: 12 |
| Country: Number of subjects enrolled | United States: 90 |
| Worldwide total number of subjects | 124 |
| EEA total number of subjects | 12 |

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) | 66 |
| From 65 to 84 years | 58 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 150 subjects were planned to enroll but 124 subjects were enrolled and analyzed in this study. Out of them, 59 subjects were enrolled in Part 1 and 65 subjects were enrolled in Part 2.

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 | Daratumumab 8 mg/kg |

Arm description:

Daratumumab 8 milligram per kilogram (mg/kg) every 4 weeks (Q4W) via intravenous (IV) route until disease progression or unacceptable toxicity.

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

Dosage and administration details:

Daratumumab 8 mg/kg Q4W as intravenous infusion.

| | |
|------------------|----------------------|
| Arm title | Daratumumab 16 mg/kg |
|------------------|----------------------|

Arm description:

Daratumumab 16 mg/kg weekly for 8 weeks; then every 2 weeks (Q2W) for 16 weeks; then Q4W via IV route until disease progression or unacceptable toxicity.

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

Dosage and administration details:

Daratumumab 16 mg/kg weekly for 8 weeks; then Q2W for 16 weeks; then Q4W until disease progression or unacceptable toxicity.

| Number of subjects in period 1 | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg |
|---------------------------------------|---------------------|----------------------|
| Started | 18 | 106 |
| Completed | 0 | 0 |
| Not completed | 18 | 106 |
| Consent withdrawn by subject | 2 | 7 |
| Other: study terminated by sponsor | 1 | 22 |
| Lost to follow-up | - | 8 |
| Other: death | 15 | 69 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | Daratumumab 8 mg/kg |
| Reporting group description: Daratumumab 8 milligram per kilogram (mg/kg) every 4 weeks (Q4W) via intravenous (IV) route until disease progression or unacceptable toxicity. | |
| Reporting group title | Daratumumab 16 mg/kg |
| Reporting group description: Daratumumab 16 mg/kg weekly for 8 weeks; then every 2 weeks (Q2W) for 16 weeks; then Q4W via IV route until disease progression or unacceptable toxicity. | |

| Reporting group values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | Total |
|---|---------------------|----------------------|-------|
| Number of subjects | 18 | 106 | 124 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 8 | 58 | 66 |
| From 65 to 84 years | 10 | 48 | 58 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 64.2 | 62.9 | |
| standard deviation | ± 7.72 | ± 10 | - |
| Title for Gender Units: subjects | | | |
| Female | 6 | 54 | 60 |
| Male | 12 | 52 | 64 |
| Stage of Disease (ISS) | | | |
| The International Staging System (ISS) system consists of stage I: beta2-microglobulin less than (<)3.5 milligram/liter (mg/l) and albumin greater than or equal to (>=) 3.5 gram (g)/100 ml; stage II: neither stage I nor stage III and stage III: beta2-microglobulin >= 5.5 mg/l. | | | |
| Units: Subjects | | | |
| stage I | 2 | 26 | 28 |
| stage II | 8 | 40 | 48 |
| stage III | 8 | 40 | 48 |
| Number of Prior Lines of Therapy Units: Subjects | | | |
| <= 3 Lines | 6 | 19 | 25 |
| > 3 Lines | 12 | 87 | 99 |
| Refractory to Proteasome Inhibitor (PI)/ Immunomodulatory Drug (IMiD) Units: Subjects | | | |
| Both a PI and IMiD | 15 | 101 | 116 |
| PI only | 1 | 3 | 4 |
| IMiD only | 0 | 1 | 1 |
| None | 2 | 1 | 3 |
| Region of Enrollment Units: Subjects | | | |

| | | | |
|---------------|----|----|----|
| Canada | 0 | 22 | 22 |
| Spain | 3 | 9 | 12 |
| United States | 15 | 75 | 90 |

End points

End points reporting groups

| | |
|---|----------------------|
| Reporting group title | Daratumumab 8 mg/kg |
| Reporting group description: Daratumumab 8 milligram per kilogram (mg/kg) every 4 weeks (Q4W) via intravenous (IV) route until disease progression or unacceptable toxicity. | |
| Reporting group title | Daratumumab 16 mg/kg |
| Reporting group description: Daratumumab 16 mg/kg weekly for 8 weeks; then every 2 weeks (Q2W) for 16 weeks; then Q4W via IV route until disease progression or unacceptable toxicity. | |

Primary: Percentage of Subjects With Overall Response

| | |
|--|---|
| End point title | Percentage of Subjects With Overall Response ^[1] |
| End point description: Overall response defined as percentage of subjects who achieved complete response (sCR), complete response (CR), very good partial response (VGPR) or (partial response)PR. Per IMWG criteria, sCR: defined as normal (free light chain) FLC ratio, and PCs by immunohistochemistry, immunofluorescence or 2- to 4-color flow cytometry; CR: Negative immunofixation on serum, urine and disappearance of tissue plasmacytomas and < 5% plasma cells in bone marrow; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥ 90% reduction in serum M-protein plus urine M-protein level < 100mg/24 hrs; PR: ≥ 50% reduction of serum M-protein and reduction in 24 hrs urinary M-protein by ≥ 90% or to <200 mg/24 hrs; if serum and urine M-protein are not measurable, decrease of ≥50% in difference between involved and uninvolved FLC levels is required in place of M-protein criteria. All treated analysis set included all subjects who received at least 1 dose of daratumumab. | |
| End point type | Primary |
| End point timeframe: Up to 14.4 Months | |
| 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 statistical analysis was performed for this endpoint. | |

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 106 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 11.1 (1.4 to 34.7) | 29.2 (20.8 to 38.9) | | |

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 calculated from the date of initial documentation of a response (PR or better) | |

to the date of first documented evidence of progressive disease, as defined in IMWG criteria. Disease progression (IMWG criteria): increase of 25 percent (%) from lowest response level in Serum M-component (the absolute increase must be ≥ 0.5 g/dL) and/or; urine M-component (the absolute increase must be ≥ 200 mg/24 hours) and/or; only in subjects without measurable serum and urine M-protein levels: the difference between involved and uninvolved free light chain levels (absolute increase must be >10 milligram per deciliter (mg/dL); Development of hypercalcemia (corrected serum calcium >11.5 mg/dL or 2.65 millimole per liter [mmol/L]) that can be attributed solely to the plasma cell proliferative disorder. Responders in all treated analysis set. Only those subjects with confirmed PR and those who experienced progressive disease (PD) were analyzed.

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

End point timeframe:

Up to 14.4 Months

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 ^[2] | 31 ^[3] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 99999 (1.8 to 99999) | 7.4 (5.5 to 99999) | | |

Notes:

[2] - 99999: Median and UL of CI were inestimable due to less responders either progressed/died due to PD

[3] - 99999: Upper limit of CI was inestimable due to less responders either progressed or died due to PD

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall Survival (OS) was defined as the number of days from administration of the first infusion (Day 1) to date of death. Median Overall Survival was estimated by using the Kaplan-Meier method. All treated analysis set included all subjects who received at least 1 dose of daratumumab.

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

End point timeframe:

Approximately up to 3 years

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 106 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 19.45 (7.72 to 26.81) | 18.60 (13.67 to 25.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Benefit

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Clinical Benefit |
|-----------------|--|

End point description:

Clinical benefit rate defined as percentage of subjects who achieved minimal response (MR) or better. MR: $\geq 25\%$ but $\leq 49\%$ reduction of serum M-protein and reduction in urine M-protein by 50%-89%. If present at baseline 25% to 49% reduction in size of soft tissue plasmacytomas. All treated analysis set included all subjects who received at least 1 dose of daratumumab.

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

End point timeframe:

Up to 14.4 Months

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 106 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 22.2 (6.4 to 47.6) | 34.0 (25.0 to 43.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

| | |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response was defined as the time from the date of first dose of daratumumab to the date of initial documentation of a response (PR or better). Responders in all treated analysis set. Only those subjects with confirmed PR were analyzed.

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

End point timeframe:

Up to 14.4 Months

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|-------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 | 31 | | |
| Units: months | | | | |
| median (full range (min-max)) | 0.99 (0.95 to 1.02) | 0.99 (0.9 to 5.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression Free Survival |
|-----------------|---------------------------|

End point description:

Progression free survival (PFS) was defined as the time between the date of first dose of daratumumab and either disease progression or death, whichever occurs first. PD as per IMWG criteria: increase of $\geq 25\%$ from lowest response level in Serum M-component and/or (absolute increase must be ≥ 0.5 gram/deciliter [g/dL]) Urine M-component and/or (absolute increase must be ≥ 200 mg/24hr; only in subjects without measurable serum, urine M-protein levels: difference b/w involved, uninvolved FLC levels. Absolute increase must be > 10 mg/dL; Bone marrow plasma cell%: absolute% must be $\geq 10\%$; Definite development of new bone lesions/soft tissue plasmacytomas/definite increase in size of existing bone lesions or soft tissue plasmacytomas; Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol/liter [mmol/L]) that can be attributed solely to plasma cell proliferative disorder. All treated analysis set included all subjects who received at least 1 dose of

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

End point timeframe:

Up to 14.4 Months

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 ^[4] | 106 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.86 (1.84 to 99999) | 3.65 (2.76 to 4.63) | | |

Notes:

[4] - 99999: Upper limit of CI was not estimable due to the relatively short duration of follow-up.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression

| | |
|-----------------|-----------------------------|
| End point title | Time to Disease Progression |
|-----------------|-----------------------------|

End point description:

Time to progression was defined as the number of days from the date of first dose of daratumumab to the date of first record of disease progression. All treated analysis set included all subjects who received at least 1 dose of daratumumab.

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

End point timeframe:

Up to 14.4 Months

| End point values | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | | |
|----------------------------------|-------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 ^[5] | 106 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.86 (1.84 to 99999) | 3.71 (2.79 to 5.39) | | |

Notes:

[5] - 99999: Median and upper limit for CI was not estimable' due to less number of subjects with events.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately up to 3.8 years

Adverse event reporting additional description:

All treated analysis set included all subjects who received at least 1 dose of daratumumab.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | Daratumumab 8 mg/kg |
|-----------------------|---------------------|

Reporting group description:

Daratumumab 8 milligram per kilogram (mg/kg) every 4 weeks (Q4W) via intravenous (IV) route until disease progression or unacceptable toxicity.

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

Reporting group description:

Daratumumab 16 mg/kg weekly for 8 weeks; then every 2 weeks (Q2W) for 16 weeks; then Q4W via IV until disease progression or unacceptable toxicity.

| Serious adverse events | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | |
|---|---------------------|----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 33 / 106 (31.13%) | |
| number of deaths (all causes) | 15 | 69 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Plasma Cell Leukaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|--|----------------|-----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General Physical Health Deterioration | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 5 / 106 (4.72%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 5 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Pelvic Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (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 | | | |
| Acute Pulmonary Oedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural Effusion | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Aspiration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood Creatinine Increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oxygen Saturation Abnormal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 | | | |
| Spinal Compression Fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural Haematoma | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|-----------------|--|
| Cardiac disorders | | | |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-Respiratory Arrest | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Cord Compression | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecal Incontinence | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic Failure | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|-----------------|--|
| Acute Kidney Injury | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Retention | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological Fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|-----------------|--|
| Spinal Column Stenosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| H1n1 Influenza | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Zoster | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar Pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parainfluenzae Virus Infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 4 / 106 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Streptococcal | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft Tissue Infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| 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 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicella | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 4 / 106 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hyperkalaemia | | | |

| | | | |
|---|----------------|-----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 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 | Daratumumab 8 mg/kg | Daratumumab 16 mg/kg | |
|---|---------------------|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 18 (100.00%) | 105 / 106 (99.06%) | |
| Vascular disorders | | | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences (all) | 1 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 8 / 18 (44.44%) | 12 / 106 (11.32%) | |
| occurrences (all) | 9 | 18 | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 6 / 106 (5.66%) | |
| occurrences (all) | 2 | 6 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 12 / 106 (11.32%) | |
| occurrences (all) | 2 | 13 | |
| Chest Discomfort | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 3 | |
| Chills | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 10 / 106 (9.43%) | |
| occurrences (all) | 7 | 10 | |
| Fatigue | | | |

| | | | |
|--|----------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 6 / 18 (33.33%) 6 | 42 / 106 (39.62%) 47 | |
| Non-Cardiac Chest Pain subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 2 | 6 / 106 (5.66%) 6 | |
| Oedema subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 2 / 106 (1.89%) 3 | |
| Oedema Peripheral subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 3 | 9 / 106 (8.49%) 12 | |
| Pain subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 6 / 106 (5.66%) 6 | |
| Pyrexia subjects affected / exposed occurrences (all) | 5 / 18 (27.78%) 5 | 20 / 106 (18.87%) 22 | |
| Immune system disorders Cytokine Release Syndrome subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Reproductive system and breast disorders Nipple Pain subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 2 | |
| Prostatitis subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 6 / 18 (33.33%) 9 | 27 / 106 (25.47%) 32 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 18 (16.67%) 5 | 18 / 106 (16.98%) 18 | |
| Dyspnoea Exertional | | | |

| | | | |
|-----------------------------|-----------------|-------------------|--|
| subjects affected / exposed | 1 / 18 (5.56%) | 9 / 106 (8.49%) | |
| occurrences (all) | 1 | 9 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 9 / 106 (8.49%) | |
| occurrences (all) | 0 | 10 | |
| Nasal Congestion | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 22 / 106 (20.75%) | |
| occurrences (all) | 2 | 26 | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 9 / 106 (8.49%) | |
| occurrences (all) | 1 | 11 | |
| Pleural Effusion | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 3 | |
| Productive Cough | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 8 / 106 (7.55%) | |
| occurrences (all) | 1 | 9 | |
| Throat Irritation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 7 / 106 (6.60%) | |
| occurrences (all) | 0 | 7 | |
| Wheezing | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 7 / 106 (6.60%) | |
| occurrences (all) | 1 | 7 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 8 / 106 (7.55%) | |
| occurrences (all) | 0 | 8 | |
| Confusional State | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 7 / 106 (6.60%) | |
| occurrences (all) | 1 | 8 | |
| Depression | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 3 | |
| Mental Status Changes | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|--|----------------------|-----------------------|--|
| Nervousness subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Investigations | | | |
| Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 4 / 106 (3.77%) 4 | |
| Blood Alkaline Phosphatase Increased subjects affected / exposed occurrences (all) | 3 / 18 (16.67%) 3 | 4 / 106 (3.77%) 4 | |
| Blood Creatinine Increased subjects affected / exposed occurrences (all) | 7 / 18 (38.89%) 7 | 9 / 106 (8.49%) 21 | |
| Blood Urea Increased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Gamma-Glutamyltransferase Increased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 1 | |
| Transaminases Increased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Weight Decreased subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 5 / 106 (4.72%) 6 | |
| Weight Increased subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 4 / 106 (3.77%) 5 | |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 2 | 5 / 106 (4.72%) 6 | |
| Cardiac disorders | | | |

| | | | |
|---|----------------------|-------------------------|--|
| Sinus Tachycardia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 1 | |
| Tachycardia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 3 / 106 (2.83%) 3 | |
| Nervous system disorders | | | |
| Anaesthesia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 10 / 106 (9.43%) 12 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 3 / 106 (2.83%) 3 | |
| Encephalopathy subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 13 / 106 (12.26%) 17 | |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 6 / 106 (5.66%) 7 | |
| Peripheral Sensory Neuropathy subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 6 / 106 (5.66%) 7 | |
| Sciatica subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Tremor subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 3 | 2 / 106 (1.89%) 2 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|-----------------------------|-----------------|-------------------|--|
| Anaemia | | | |
| subjects affected / exposed | 9 / 18 (50.00%) | 39 / 106 (36.79%) | |
| occurrences (all) | 20 | 101 | |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 8 / 106 (7.55%) | |
| occurrences (all) | 2 | 18 | |
| Lymphopenia | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 5 / 106 (4.72%) | |
| occurrences (all) | 6 | 10 | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 26 / 106 (24.53%) | |
| occurrences (all) | 4 | 56 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 28 / 106 (26.42%) | |
| occurrences (all) | 17 | 71 | |
| Ear and labyrinth disorders | | | |
| Cerumen Impaction | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear Discomfort | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences (all) | 1 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal Discomfort | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 4 | |
| Abdominal Distension | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 3 | |
| Abdominal Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 7 / 106 (6.60%) | |
| occurrences (all) | 1 | 8 | |
| Aphthous Stomatitis | | | |

| | | | |
|--|-----------------|-------------------|--|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 19 / 106 (17.92%) | |
| occurrences (all) | 1 | 21 | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 22 / 106 (20.75%) | |
| occurrences (all) | 5 | 31 | |
| Dry Mouth | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 34 / 106 (32.08%) | |
| occurrences (all) | 5 | 39 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 19 / 106 (17.92%) | |
| occurrences (all) | 2 | 22 | |
| Hepatobiliary disorders | | | |
| Hepatic Steatosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic Keratosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nail Discolouration | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 106 (2.83%) | |
| occurrences (all) | 1 | 3 | |
| Rash | | | |

| | | | |
|---|----------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 2 / 106 (1.89%) 2 | |
| Rash Macular subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 1 | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 1 | |
| Renal and urinary disorders Bladder Spasm subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Haematuria subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 2 / 106 (1.89%) 2 | |
| Micturition Urgency subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Urinary Incontinence subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 1 / 106 (0.94%) 1 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 20 / 106 (18.87%) 23 | |
| Back Pain subjects affected / exposed occurrences (all) | 5 / 18 (27.78%) 5 | 25 / 106 (23.58%) 27 | |
| Bone Pain subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 10 / 106 (9.43%) 12 | |
| Flank Pain subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Muscle Spasms | | | |

| | | | |
|-----------------------------------|-----------------|-------------------|--|
| subjects affected / exposed | 2 / 18 (11.11%) | 9 / 106 (8.49%) | |
| occurrences (all) | 3 | 10 | |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 15 / 106 (14.15%) | |
| occurrences (all) | 2 | 16 | |
| Musculoskeletal Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 12 / 106 (11.32%) | |
| occurrences (all) | 1 | 14 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 6 / 106 (5.66%) | |
| occurrences (all) | 0 | 8 | |
| Pain in Extremity | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 20 / 106 (18.87%) | |
| occurrences (all) | 1 | 22 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 7 / 106 (6.60%) | |
| occurrences (all) | 0 | 9 | |
| Candida Infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 106 (0.94%) | |
| occurrences (all) | 1 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 4 / 106 (3.77%) | |
| occurrences (all) | 2 | 4 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 8 / 106 (7.55%) | |
| occurrences (all) | 1 | 11 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 4 / 106 (3.77%) | |
| occurrences (all) | 1 | 5 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 7 / 106 (6.60%) | |
| occurrences (all) | 1 | 11 | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 21 / 106 (19.81%) | |
| occurrences (all) | 3 | 32 | |

| | | | |
|---|----------------------|-------------------------|--|
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 7 / 106 (6.60%) 7 | |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 4 | 19 / 106 (17.92%) 21 | |
| Fluid Retention subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 106 (0.00%) 0 | |
| Hypercalcaemia subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 4 | 16 / 106 (15.09%) 28 | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 3 / 18 (16.67%) 3 | 9 / 106 (8.49%) 15 | |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 3 / 106 (2.83%) 3 | |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 4 / 106 (3.77%) 4 | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 5 | 5 / 106 (4.72%) 6 | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 2 | 3 / 106 (2.83%) 9 | |
| Hypoglycaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 106 (0.94%) 3 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 4 | 11 / 106 (10.38%) 17 | |
| Hypomagnesaemia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 18 (11.11%) | 8 / 106 (7.55%) | |
| occurrences (all) | 2 | 19 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 7 / 106 (6.60%) | |
| occurrences (all) | 7 | 7 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolic Acidosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 106 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 26 November 2013 | The overall reason for the amendment was to include the following changes: the sample size was increased to approximately 20 subjects per treatment group in Part 1 Stage 1 from an original 15 subjects, the study agent administration guidelines were changed from mg/hr to mL/hr, and minor additional changes were made for clarification throughout the protocol. |
| 07 February 2014 | The overall reason for the amendment was to include the following changes: following the discontinuation of the dose schedule of 8 mg/kg every 4 weeks (Treatment Group B) at the end of Stage 1, the number of subjects in Part 2 was increased to approximately 60 subjects, biomarker sampling time points were modified, and subjects in Group B were allowed to crossover to Group A. |
| 09 July 2014 | The overall reason for the amendment was to change the timing of the on treatment bone marrow biopsy. |
| 08 June 2015 | The overall reason for the amendment was to allow subjects who are benefiting from daratumumab to continue to receive study treatment beyond the previously defined end of study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported