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 (Ctrough).

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 (Ctrough) of Daratumumab

End point title	Maximum Trough Concentration (Ctrough) of Daratumumab[1]

End point description:

Maximum Ctrough 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 (>=) 50 percent (%) reduction of serum M-protein and reduction in 24-hour urinary M-protein by >=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), immunofluorescencea 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 >=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, immunofluorescencea 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 >=0.5g/dL and >=200mg/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 >10mg/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 >11.5mg/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	15 / 260 (5.77%)	11 / 258 (4.26%)	
occurrences (all)	20	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	16 / 260 (6.15%)	22 / 258 (8.53%)	
occurrences (all)	17	26	
Diarrhoea			
subjects affected / exposed	41 / 260 (15.77%)	32 / 258 (12.40%)	
occurrences (all)	64	50	
Nausea			
subjects affected / exposed	24 / 260 (9.23%)	31 / 258 (12.02%)	
occurrences (all)	29	37	
Vomiting			
subjects affected / exposed	16 / 260 (6.15%)	21 / 258 (8.14%)	
occurrences (all)	17	24	
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed	10 / 260 (3.85%)	13 / 258 (5.04%)	
occurrences (all)	11	13	
Dyspnoea			
subjects affected / exposed	15 / 260 (5.77%)	28 / 258 (10.85%)	
occurrences (all)	19	34	
Cough			
subjects affected / exposed	25 / 260 (9.62%)	36 / 258 (13.95%)	
occurrences (all)	39	37	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 260 (5.38%)	14 / 258 (5.43%)	
occurrences (all)	15	15	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	33 / 260 (12.69%)	18 / 258 (6.98%)	
occurrences (all)	40	20	
Back Pain			
subjects affected / exposed	31 / 260 (11.92%)	36 / 258 (13.95%)	
occurrences (all)	48	42	
Bone Pain			
subjects affected / exposed	17 / 260 (6.54%)	10 / 258 (3.88%)	
occurrences (all)	17	12	

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