Clinical trial results:
Phase 3 Study Comparing Daratumumab, Bortezomib and Dexamethasone (DVd) vs Bortezomib and Dexamethasone (Vd) in Subjects With Relapsed or Refractory Multiple Myeloma

Summary

EudraCT number	2014-000255-85
Trial protocol	DE SE ES CZ NL HU IT PL
Global end of trial date	28 June 2021

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	54767414MMY3004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02136134
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920, US Highway 202, South Raritan, NJ, 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	28 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2021
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 to compare the efficacy of daratumumab, VELCADE (bortezomib) and dexamethasone (DVd) to that of bortezomib and dexamethasone (Vd), in terms of progression-free survival (PFS) in subjects with relapsed or refractory multiple myeloma.

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 Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2014
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: 43
Country: Number of subjects enrolled	Brazil: 22
Country: Number of subjects enrolled	Czechia: 35
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Netherlands: 25
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	Sweden: 19
Country: Number of subjects enrolled	Turkey: 28
Country: Number of subjects enrolled	Ukraine: 50
Country: Number of subjects enrolled	United States: 37
Worldwide total number of subjects	498
EEA total number of subjects	263

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)	257
From 65 to 84 years	239
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 498 subjects were enrolled and received the study treatments.

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	Bortezomib + Dexamethasone (Vd)

Arm description:

Subjects received bortezomib 1.3 milligrams per square metre (mg/m^2) subcutaneous (SC) injection on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 milligrams (mg) orally (PO) on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles. Subjects who met sponsor-confirmed disease progression eligibility criteria received daratumumab monotherapy) as a subsequent antimyeloma therapy as follow: daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion or daratumumab SC injection (1800 mg fixed dose) weekly for the first 2 cycles, every 2 weeks from Cycle 3 to 6, and then every 4 weeks thereafter.

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received dexamethasone 20 mg on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	VELCADE
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received bortezomib 1.3 mg/m^2 on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles).

Arm title	Daratumumab + Bortezomib and Dexamethasone (DVd)

Arm description:

Subjects received daratumumab 16 mg/kg IV infusion weekly or daratumumab SC injection (1800 mg fixed dose) for the first 3 cycles, on Day 1 of Cycles 4-8, and then every 4 weeks thereafter, bortezomib 1.3 mg/m^2 SC injection administration on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 mg orally on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.

Arm type	Experimental

Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects received daratumumab 16 mg/kg SC infusion weekly or IV for the first 3 cycles, on Day 1 of Cycles 4-8, and then every 4 weeks thereafter.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received dexamethasone 20 mg on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	VELCADE
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received bortezomib 1.3 mg/m^2 on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles).

Number of subjects in period 1	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)
Started	247	251
Completed	0	0
Not completed	247	251
Adverse event, serious fatal	170	148
Consent withdrawn by subject	19	10
Uspecified	55	90
Lost to follow-up	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Bortezomib + Dexamethasone (Vd)
Reporting group description:	
Subjects received bortezomib 1.3 milligrams per square metre (mg/m^2) subcutaneous (SC) injection on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 milligrams (mg) orally (PO) on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles. Subjects who met sponsor-confirmed disease progression eligibility criteria received daratumumab monotherapy) as a subsequent antimyeloma therapy as follow: daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion or daratumumab SC injection (1800 mg fixed dose) weekly for the first 2 cycles, every 2 weeks from Cycle 3 to 6, and then every 4 weeks thereafter.	
Reporting group title	Daratumumab + Bortezomib and Dexamethasone (DVd)
Reporting group description:	
Subjects received daratumumab 16 mg/kg IV infusion weekly or daratumumab SC injection (1800 mg fixed dose) for the first 3 cycles, on Day 1 of Cycles 4-8, and then every 4 weeks thereafter, bortezomib 1.3 mg/m^2 SC injection administration on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 mg orally on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.	

Reporting group values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)	Total
Number of subjects	247	251	498
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	125	132	257
From 65-84 years	121	118	239
85 years and over	1	1	2
Age continuous Units: years			
arithmetic mean	63.9	62.8	
standard deviation	± 9.81	± 9.66	-
Sex: Female, Male Units: subjects			
Female	99	114	213
Male	148	137	285
Stage of Disease (ISS) Units: Subjects			
Category: I	96	98	194
Category: II	100	94	194
Category: III	51	59	110
No. of Prior Lines of Therapy Units: Subjects			

Therapy: 1	113	122	235
Therapy: 2	74	70	144
Therapy: 3	32	37	69
Therapy: >3	28	22	50
Region of Enrollment Units: Subjects			
Australia	20	23	43
Brazil	9	13	22
Czech Republic	19	16	35
Germany	21	21	42
Hungary	14	16	30
Italy	25	24	49
Korea, Republic of	8	10	18
Mexico	1	2	3
Netherlands	14	11	25
Poland	18	16	34
Russian Federation	13	21	34
Spain	19	10	29
Sweden	9	10	19
Turkey	14	14	28
Ukraine	22	28	50
United States	21	16	37

End points

End points reporting groups

Reporting group title	Bortezomib + Dexamethasone (Vd)

Reporting group description:

Subjects received bortezomib 1.3 milligrams per square metre (mg/m^2) subcutaneous (SC) injection on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 milligrams (mg) orally (PO) on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles. Subjects who met sponsor-confirmed disease progression eligibility criteria received daratumumab monotherapy) as a subsequent antimyeloma therapy as follow: daratumumab 16 milligrams per kilogram (mg/kg) intravenous (IV) infusion or daratumumab SC injection (1800 mg fixed dose) weekly for the first 2 cycles, every 2 weeks from Cycle 3 to 6, and then every 4 weeks thereafter.

Reporting group title	Daratumumab + Bortezomib and Dexamethasone (DVd)

Reporting group description:

Subjects received daratumumab 16 mg/kg IV infusion weekly or daratumumab SC injection (1800 mg fixed dose) for the first 3 cycles, on Day 1 of Cycles 4-8, and then every 4 weeks thereafter, bortezomib 1.3 mg/m^2 SC injection administration on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 mg orally on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.

Primary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[1]

End point description:

PFS:duration from date of randomisation to either progressive disease (PD)/death, whichever occurred first. PD:meeting any one of criteria:increase of greater than equal to (>=)25 percent (%) in level of serum M-protein from lowest response value and absolute increase must be >=0.5 g/dL;increase of >=25% in 24-hour urine M-protein from lowest response value and absolute increase must be >=200 mg/24hours;only in subjects without measurable serum and urine M-protein levels: increase of >=25% in difference between involved and uninvolved FLC levels from lowest response value and absolute increase must be >10 mg/dL;definite increase in size of existing bone lesions/soft tissue PCs; definite development of new bone lesions or soft tissue PC;development of hypercalcemia (corrected serum calcium >11.5 mg/dL) that can be attributed solely to PC proliferative disorder. Intent-to-treat set:all randomised subjects.99999:median & upper limit of 95% CI not estimable due to lower number of events.

End point type	Primary

End point timeframe:

From the date of randomisation to either progressive disease or death, whichever occurred first (approximately 1 year 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 statistics was done, no inferential statistical analysis was performed.

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	251		
Units: months				
median (confidence interval 95%)	7.16 (6.21 to 7.85)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Response rate of VGPR/better:percentage of subjects achieved VGPR & CR (with sCR) as per IMWG criteria during/after treatment. IMWG criteria:Serum & urine M-component detectable by immunofixation but not on electrophoresis or >=90% reduction in serum M-protein plus urine M-protein <100 mg/24 hours, if serum & urine M-protein not measurable, decrease of >90% in difference between involved & uninvolved FLC levels required in place of M-protein criteria, in addition to above criteria, if present at baseline, >=50% reduction in size of soft tissue plasmacytomas (PC) also required; CR:Negative immunofixation on serum & urine, disappearance of any soft tissue PC, <5% PC in bone marrow; sCR:CR & normal FLC ratio, absence of clonal PCs by immunohistochemistry, immunofluorescence/2-4 color flow cytometry. Response evaluable analysis set:subjects with confirmed multiple myeloma & baseline measurable disease, had at least 1 treatment administration & at least 1 post baseline disease measure.

End point type	Secondary

End point timeframe:

Up to disease progression (approximately 9 years 10 months)

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	240		
Units: percentage of subjects				
number (confidence interval 95%)	29.1 (23.3 to 35.3)	59.2 (52.7 to 65.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression (TTP)

End point title	Time to Disease Progression (TTP)

End point description:

TTP: time from date of randomisation to date of first documented evidence of PD. PD:meeting any one of the criteria: increase of >=25% in level of serum M-protein from lowest response value and absolute increase must be >=0.5 g/dL; increase of >=25% in 24-hour urine M-protein from lowest response

value and absolute increase must be >=200 mg/24hours;only in subjects without measurable serum and urine M-protein levels:increase of >=25% in difference between involved and uninvolved FLC levels from lowest response value and absolute increase must be >10 milligram per deciliter (mg/dL);definite increase in size of existing bone lesions or soft tissue plasmacytomas; definite development of new bone lesions or soft tissue plasmacytomas; development of hypercalcemia (corrected serum calcium >11.5 mg/dL) that can be attributed solely to plasma cell (PC) proliferative disorder. Intent-to-treat analysis set. 99999:median and upper limit of 95% CI was not estimable due to lower number of events.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of first documented evidence of progression or death due to PD whichever occurred first (approximately 9 years 10 months)

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	251		
Units: months				
median (confidence interval 95%)	7.29 (6.41 to 8.08)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR:percentage of subjects who achieved stringent complete response (sCR), complete response (CR), VGPR, or partial response (PR) according to the IMWG criteria, during the study or during follow up. IMWG criteria for PR: >=50% reduction of serum M-protein and reduction in 24 hour urinary M-protein by >=90% or to <200 mg/24 hours, if the serum and urine M-protein are not measurable, a decrease of >=50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria, in addition to the above criteria, if present at baseline, a >=50% reduction in the size of soft tissue plasmacytomas is also required. Response-evaluable analysis set: subjects who had confirmed diagnosis of multiple myeloma and measurable disease at baseline or screening visit, received at least 1 administration of study treatment and had at least 1 post baseline disease assessment. Here, N (number of subjects analysed) refers to number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to disease progression (approximately 9 years 10 months)

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	240		
Units: percentage of subjects				
number (confidence interval 95%)	63.2 (56.7 to 69.4)	82.9 (77.5 to 87.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival was measured from the date of randomisation to the date of the subject's death. The intent-to-treat population included all randomised subjects.

End point type	Secondary

End point timeframe:

Up to the end of the study (approximately 9 years 10 months)

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	251		
Units: months				
median (confidence interval 95%)	38.51 (31.18 to 46.23)	49.58 (42.18 to 62.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Negative Minimal Residual Disease (MRD)

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

End point description:

The MRD negativity rate was defined as the percentage of subjects who had negative MRD assessment at any timepoint after the first dose of study drugs by evaluation of bone marrow aspirates or whole blood. MRD was assessed in subjects who achieved complete response or stringent complete response (CR/sCR). IMWG criteria for CR: Negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas, and <5% PCs in bone marrow; sCR: CR plus normal FLC ratio, absence of clonal PCs by immunohistochemistry, immunofluorescence or 2 to 4 color flow cytometry. The intent-to-

treat population included all randomised subjects.

End point type	Secondary

End point timeframe:

Up to disease progression (approximately 9 years 10 months)

End point values	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	251		
Units: percentage of subjects				
number (not applicable)	2.8	13.5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 9 years 10 months

Adverse event reporting additional description:

Safety population included all randomised subjects who had at least 1 administration of any of the study treatment (partial or complete).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Bortezomib + Dexamethasone (Vd)

Reporting group description:

Subjects received bortezomib 1.3 milligrams per square metre (mg/m^2) subcutaneous (SC) injection on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 milligrams (mg) orally (PO) on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles. Subjects who met sponsor-confirmed disease progression eligibility criteria received daratumumab monotherapy) as a subsequent antimyeloma therapy.

Reporting group title	Daratumumab + Bortezomib and Dexamethasone (DVd)

Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) intravenous (IV) infusion weekly or daratumumab SC injection (1800 mg fixed dose) for the first 3 cycles, on Day 1 of Cycles 4-8, and then every 4 weeks thereafter, bortezomib 1.3 mg/m^2 SC injection administration on Days 1, 4, 8, and 11 of each 21-day cycle (8 treatment cycles) and dexamethasone 20 mg orally on Days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles.

Serious adverse events	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)	
Total subjects affected by serious adverse events			
subjects affected / exposed	81 / 237 (34.18%)	134 / 243 (55.14%)	
number of deaths (all causes)	171	148	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Basal cell carcinoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential thrombocythaemia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tract adenoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmablastic lymphoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery aneurysm			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	2 / 237 (0.84%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 237 (1.27%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	3 / 237 (1.27%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 237 (1.27%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 237 (1.69%)	7 / 243 (2.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 237 (0.00%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Organising pneumonia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 237 (0.00%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 237 (0.00%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal swelling			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			

subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 237 (0.84%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 237 (0.84%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT interval abnormal			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Avulsion fracture			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 237 (0.00%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 237 (0.42%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 237 (0.42%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 237 (0.00%)	6 / 243 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 237 (0.42%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 237 (0.84%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 237 (0.42%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 237 (0.00%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless legs syndrome			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 237 (0.84%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIth nerve paralysis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 237 (0.42%)	9 / 243 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 237 (0.42%)	6 / 243 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 237 (1.27%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	3 / 237 (1.27%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 237 (0.00%)	4 / 243 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			

subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous ulcer			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloma cast nephropathy			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 237 (0.42%)	4 / 243 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 237 (0.84%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 237 (0.84%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 237 (0.42%)	4 / 243 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Flank pain			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gangrene			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 237 (0.84%)	7 / 243 (2.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal oesophagitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	3 / 237 (1.27%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophilus bacteraemia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 237 (0.84%)	3 / 243 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 237 (0.84%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 237 (0.84%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraspinal abscess			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	24 / 237 (10.13%)	26 / 243 (10.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			

subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary nocardiosis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 237 (0.84%)	4 / 243 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 237 (0.84%)	6 / 243 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia serratia			

subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 237 (0.00%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 237 (0.84%)	2 / 243 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	2 / 237 (0.84%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 237 (0.42%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 237 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 237 (0.84%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	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	Bortezomib + Dexamethasone (Vd)	Daratumumab + Bortezomib and Dexamethasone (DVd)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	217 / 237 (91.56%)	238 / 243 (97.94%)	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 237 (2.11%)	15 / 243 (6.17%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	10 / 237 (4.22%)	20 / 243 (8.23%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	3 / 237 (1.27%)	19 / 243 (7.82%)	
occurrences (all)	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	10 / 237 (4.22%)	13 / 243 (5.35%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	8 / 237 (3.38%)	30 / 243 (12.35%)	
occurrences (all)	0	0	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	14 / 237 (5.91%)	13 / 243 (5.35%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	26 / 237 (10.97%)	34 / 243 (13.99%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	14 / 237 (5.91%)	29 / 243 (11.93%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	25 / 237 (10.55%)	31 / 243 (12.76%)	
occurrences (all)	0	0	

Peripheral sensory neuropathy			
subjects affected / exposed	90 / 237 (37.97%)	122 / 243 (50.21%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	105 / 237 (44.30%)	145 / 243 (59.67%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	23 / 237 (9.70%)	47 / 243 (19.34%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	9 / 237 (3.80%)	33 / 243 (13.58%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	12 / 237 (5.06%)	23 / 243 (9.47%)	
occurrences (all)	0	0	
Anaemia			
subjects affected / exposed	75 / 237 (31.65%)	68 / 243 (27.98%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	36 / 237 (15.19%)	27 / 243 (11.11%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	58 / 237 (24.47%)	57 / 243 (23.46%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	9 / 237 (3.80%)	13 / 243 (5.35%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	20 / 237 (8.44%)	48 / 243 (19.75%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	26 / 237 (10.97%)	42 / 243 (17.28%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	37 / 237 (15.61%)	56 / 243 (23.05%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	10 / 237 (4.22%)	14 / 243 (5.76%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	53 / 237 (22.36%)	88 / 243 (36.21%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	13 / 237 (5.49%)	9 / 243 (3.70%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	27 / 237 (11.39%)	37 / 243 (15.23%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	9 / 237 (3.80%)	30 / 243 (12.35%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	7 / 237 (2.95%)	19 / 243 (7.82%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	12 / 237 (5.06%)	12 / 243 (4.94%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	21 / 237 (8.86%)	47 / 243 (19.34%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	30 / 237 (12.66%)	71 / 243 (29.22%)	
occurrences (all)	0	0	
Bronchospasm			
subjects affected / exposed	1 / 237 (0.42%)	23 / 243 (9.47%)	
occurrences (all)	0	0	
Throat irritation			

subjects affected / exposed	1 / 237 (0.42%)	13 / 243 (5.35%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	3 / 237 (1.27%)	13 / 243 (5.35%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	3 / 237 (1.27%)	14 / 243 (5.76%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 237 (2.95%)	16 / 243 (6.58%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	36 / 237 (15.19%)	44 / 243 (18.11%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	16 / 237 (6.75%)	33 / 243 (13.58%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	4 / 237 (1.69%)	15 / 243 (6.17%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	4 / 237 (1.69%)	25 / 243 (10.29%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	5 / 237 (2.11%)	25 / 243 (10.29%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	13 / 237 (5.49%)	21 / 243 (8.64%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	24 / 237 (10.13%)	52 / 243 (21.40%)	
occurrences (all)	0	0	
Arthralgia			

subjects affected / exposed	14 / 237 (5.91%)	48 / 243 (19.75%)	
occurrences (all)	0	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	8 / 237 (3.38%)	26 / 243 (10.70%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	14 / 237 (5.91%)	35 / 243 (14.40%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	5 / 237 (2.11%)	21 / 243 (8.64%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	41 / 237 (17.30%)	88 / 243 (36.21%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	9 / 237 (3.80%)	22 / 243 (9.05%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	9 / 237 (3.80%)	33 / 243 (13.58%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	6 / 237 (2.53%)	17 / 243 (7.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	5 / 237 (2.11%)	17 / 243 (7.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 237 (5.06%)	28 / 243 (11.52%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	17 / 237 (7.17%)	22 / 243 (9.05%)	
occurrences (all)	0	0	
Hypocalcaemia			

subjects affected / exposed	11 / 237 (4.64%)	17 / 243 (7.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	11 / 237 (4.64%)	26 / 243 (10.70%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	7 / 237 (2.95%)	17 / 243 (7.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 April 2016	The purpose was that following positive interim analysis # 2 results, subjects who were randomized to the VELCADE-dexamethasone (Vd) group and who have sponsor-confirmed disease progression will be offered treatment with daratumumab monotherapy (within this amendment referred to as the "Daratumumab Monotherapy Period for the Vd group"). Subjects who receive daratumumab monotherapy will have a limited schedule of assessments and limited adverse event (AE) collection.
01 November 2016	The purpose was that the International Myeloma Working Group (IMWG) had recently defined new categories of MRD–negativity. In order to align with the new categories of MRD negativity, additional time points for collection of bone marrow aspirate had been added, for purposes of MRD assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported