Clinical trial results:
An Open label, International, Multicenter, Dose Escalating Phase 1/2 Trial Investigating the Safety of Daratumumab in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma

Summary

EudraCT number	2011-005709-62
Trial protocol	NL DK GB
Global end of trial date	13 February 2017

Results information

Result version number	v1 (current)
This version publication date	07 November 2025
First version publication date	07 November 2025

Trial information

Trial identification

Sponsor protocol code	DARA-GEN503

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01615029
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., 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	23 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to establish the safety profile of daratumumab when given in combination with lenalidomide/dexamethasone in participants with relapsed or relapsed and 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	26 June 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	45
EEA total number of subjects	35

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)	45
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 45 participants were enrolled in the study, received the treatment, and were included in the analysis.

Pre-assignment

Screening details:

Adult participants aged 18 years or older who had relapsed multiple myeloma after receiving a minimum of 2 and a maximum of 4 prior lines of therapy (phase 1) and have received at least 1 prior line of therapy for multiple myeloma (phase 2) were included in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Arm description:

Participants administered with daratumumab 2 milligrams per kilogram (mg/kg) on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 milligrams (mg) on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator’s discretion). Each treatment cycle consists of 28 days.

Arm type	Experimental
Investigational medicinal product name	Daratumumab 2 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received daratumumab 2 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion).

Investigational medicinal product name	Lenalidomide 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle.

Arm title	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Arm description:

Participants administered with daratumumab 4 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator’s discretion). Each treatment cycle consists of 28 days.

Arm type	Experimental
Investigational medicinal product name	Daratumumab 4 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received daratumumab 4 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion).

Investigational medicinal product name	Lenalidomide 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle.

Arm title	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Arm description:

Participants administered with daratumumab 8 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator’s discretion). Each treatment cycle consists of 28 days.

Arm type	Experimental
Investigational medicinal product name	Daratumumab 8 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received daratumumab 8 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle

6 at the investigator's discretion).

Investigational medicinal product name	Lenalidomide 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle.

Arm title	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Arm description:

Participants administered with daratumumab 16 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator’s discretion). Each treatment cycle consists of 28 days.

Arm type	Experimental
Investigational medicinal product name	Daratumumab 16 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received daratumumab 16 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion).

Investigational medicinal product name	Lenalidomide 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle.

Arm title	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Arm description:

Participants administered with daratumumab 16 mg/kg on Days 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator’s discretion). Each treatment cycle consists of 28 days.

Arm type	Experimental
Investigational medicinal product name	Daratumumab 16 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received daratumumab 16 mg/kg on Days 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22

(cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Participants received dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion).

Investigational medicinal product name	Lenalidomide 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle.

Number of subjects in period 1	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Started	3	3	4
Completed	1	2	0
Not completed	2	1	4
Physician decision	-	-	-
Adverse event, non-fatal	1	-	3
Progressive disease	1	1	1

Number of subjects in period 1	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Started	3	32
Completed	2	16
Not completed	1	16
Physician decision	-	2
Adverse event, non-fatal	-	4
Progressive disease	1	10

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 2 milligrams per kilogram (mg/kg) on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 milligrams (mg) on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 4 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 8 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 16 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 16 mg/kg on Days 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group values	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Number of subjects	3	3	4
Age Categorical Units: Subjects			

Age continuous Units: Years			
arithmetic mean	62.7	62.7	57.5
standard deviation	± 12.74	± 2.08	± 9.68

Gender categorical Units: Participants			
Male	3	2	4
Female	0	1	0
Stage of Disease [International Staging System (ISS) Units: Subjects			
Stage I	0	1	4
Stage II	2	1	0
Stage III	1	1	0
No. of Prior Lines of Therapy Units: Subjects			
1 Line	0	0	0
2-3 Lines	2	3	3
>3 Lines	1	0	1
Refractory to Proteasome Inhibitor (PI)/ Immunomodulatory drug (IMiD) Units: Subjects			
Both a PI and IMiD	0	0	3
PI only	0	2	0
IMiD only	0	1	0
None	3	0	1

Reporting group values	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Total
Number of subjects	3	32	45
Age Categorical Units: Subjects			
Age continuous Units: Years			
arithmetic mean	67.3	59.7	
standard deviation	± 10.26	± 8.38	-
Gender categorical Units: Participants			
Male	1	22	32
Female	2	10	13
Stage of Disease [International Staging System (ISS) Units: Subjects			
Stage I	1	15	21
Stage II	1	14	18
Stage III	1	3	6
No. of Prior Lines of Therapy Units: Subjects			
1 Line	0	15	15
2-3 Lines	2	17	27
>3 Lines	1	0	3
Refractory to Proteasome Inhibitor (PI)/ Immunomodulatory drug (IMiD) Units: Subjects			

Both a PI and IMiD	1	0	4
PI only	0	5	7
IMiD only	1	1	3
None	1	26	31

End points

End points reporting groups

Reporting group title	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 2 milligrams per kilogram (mg/kg) on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 milligrams (mg) on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 4 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 8 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 16 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants administered with daratumumab 16 mg/kg on Days 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (Cycles 3 to 6), Day 1 (Cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Subject analysis set title	Phase 1: Daratumumab (2-16mg/kg)+Lenalidomide & Dexamethasone
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered Daratumumab at escalating doses of 2 mg/kg, 4 mg/kg, 8 mg/kg, or 16 mg/kg on Day 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Day 1 of Cycles 3 to 6, and Day 1 of Cycles 7 and beyond. Each cycle consisted of 28 days. Lenalidomide (25 mg was administered orally once daily on Days 1 to 21 of each 28-day cycle) and Dexamethasone (40 mg weekly) were administered concurrently. Dexamethasone dosage could be reduced to 20 mg weekly after Cycle 6 or at the investigator's discretion. Each treatment cycle consisted of 28 days.

Primary: Phase 1: Percentage of Participants With Overall Response Rate (ORR)

End point title	Phase 1: Percentage of Participants With Overall Response Rate (ORR)[1][2]

End point description:

ORR is defined as percentage of participants who achieved stringent complete response (sCR), complete response (CR), very good partial response (VGPR) or partial response (PR). International myeloma working group (IMWG) criteria (2011)- CR: Negative immunofixation on the serum and urine and

disappearance of any soft tissue plasmacytomas and less than (<) 5 percent (%) plasma cells in bone marrow; sCR: CR+Normal free light chain ratio and absence of clonal cells in bone marrow by immunohistochemistry or immuno fluorescence; PR: greater than equal to (>=) 50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by >= 90% or to <200 mg/24 hours; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level <100 mg per 24 hour. All treated analysis set included all enrolled participants who received at least one non-zero dose of any study drug during Phase 1.

End point type	Primary

End point timeframe:

Up to 3 years

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: No inferential statistics were planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	4	3
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (29.2 to 100.0)	100.0 (29.2 to 100.0)	75.0 (19.4 to 99.4)	66.7 (9.4 to 99.2)

End point values	Phase 1: Daratumumab (2-16mg/kg)+Lenalidomide & Dexamethasone			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: Percentage of participants				
number (confidence interval 95%)	85.4 (64.8 to 98.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Percentage of Participants With Overall Response Rate (ORR)

End point title	Phase 2: Percentage of Participants With Overall Response Rate (ORR)[3][4]

End point description:

ORR is defined as percentage of participants who achieved stringent complete response (sCR), complete

response (CR), very good partial response (VGPR) or partial response (PR). IMWG criteria 2011- CR: Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and less than (<) 5% plasma cells in bone marrow; sCR: CR+Normal free light chain ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence; PR: greater than eqaul to (>=) 50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by >= 90 percentage (%) or to <200 mg/24 hours; VGPR: Serum and urine Mprotein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level <100 mg per 24 hour. Intent-to-Treat (ITT) population analysis set included all enrolled participants who signed the informed consent (ICF) during Phase 2.

End point type	Primary

End point timeframe:

Up to 3 years

Notes:

[3] - 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: No inferential statistics were planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Percentage of participants				
number (not applicable)	81.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to Response

End point title	Phase 1: Time to Response[5]

End point description:

Time to first response was defined as the time from the date of first dose of daratumumab to the date of initial documentation of a response (PR or better). Time to best response was defined as the time between the date of first dose of daratumumab and the date of the initial evaluation of the best response (PR or better) to treatment. Responders in all treated population analysis set included all enrolled participants who received at least one non-zero dose of any study drug during Phase 1. Here, 'N' (overall number of participants analyzed) signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	2
Units: Months				
median (full range (min-max))				
Time to first response	0.99 (0.5 to 1.0)	1.02 (0.5 to 1.9)	1.02 (1.0 to 1.8)	2.25 (1.9 to 2.6)
Time to best response	1.9 (1.0 to 6.5)	13.17 (3.7 to 20.7)	8.41 (1.0 to 19.9)	16.72 (6.5 to 26.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response

End point title	Phase 2: Duration of Response[6]

End point description:

Duration of response was calculated from the date of initial documentation of a response (PR or better) to the date of first documented evidence of progressive disease, as defined in the IMWG criteria 2011. Responders in ITT population analysis set included. ITT population analysis set included all enrolled participants who signed the informed consent during Phase 2. Here, 'N' (overall number of participants analyzed) signifies participants evaluable for this outcome measure. Here, 99999 signifies median and 95% CI lower limit was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Months				
median (confidence interval 95%)	99999 (26.5 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Response

End point title	Phase 2: Time to Response[7]

End point description:

Time to first response was defined as the time from the date of first dose of daratumumab to the date of initial documentation of a response (PR or better). Time to best response was defined as the time between the date of first dose of daratumumab and the date of the initial evaluation of the best response (PR or better) to treatment. ITT population analysis set included all enrolled participants who signed the informed consent during Phase 2. Here, 'N' (overall number of participants analyzed) signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Months				
median (full range (min-max))				
Time to first response	0.99 (0.5 to 5.6)			
Time to best response	6.95 (0.5 to 26.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Progression (TTP)

End point title	Phase 2: Time to Progression (TTP)[8]

End point description:

TTP was defined as the number of days from the date of first infusion (Day 1) to the date of first record of disease progression. Disease progression (IMWG criteria 2011): increase of >=25% from lowest response level in serum M-component and/or (the absolute increase must be >=0.5 g/dL) urine M-component and/or (the absolute increase must be >=200 mg/24 hour; only in participants without measurable serum and urine M-protein levels: the difference between involved and uninvolved free light chain levels. The absolute increase must be >10 mg/dL; Bone marrow plasma cell percentage: the absolute % must be >=10 %; Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas. ITT population analysis set included all enrolled participants who signed the ICF during Phase 2. Here, 99999 signifies median and 95% CI lower limit was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Months				
median (confidence interval 95%)	99999 (27.0 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-Free Survival (PFS)

End point title	Phase 2: Progression-Free Survival (PFS)[9]

End point description:

Progression free survival (PFS) was defined as the time between the date of first dose of daratumumab and either disease progression or death, whichever occurs first. ITT population analysis set included all enrolled participants who signed the informed consent during Phase 2. Here, 99999 signifies median and 95% CI lower limit was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Months				
median (confidence interval 95%)	99999 (16.62 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS)[10]

End point description:

Overall Survival (OS) was defined as the number of days from administration of the first infusion (Day 1) to date of death. Median Overall Survival was estimated by using the Kaplan Meier method. ITT population analysis set included all enrolled participants who signed the informed consent during Phase 2. Here, 99999 signifies median and 95% CI lower limit was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to 5 years

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data was planned to be reported for specified baseline arms only.

End point values	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Months				
median (confidence interval 95%)	99999 (32.23 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths: From screening (Day -21) up to 5 years; Serious and Non-serious AEs: From Day 1 up to 50.4 months

Adverse event reporting additional description:

All treated analysis set included all enrolled participants who received at least one non-zero dose of any study drug during Phase 1. The safety analysis set included all enrolled participants who received at least one non-zero dose of any study drug during Phase 2.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants received daratumumab 2 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants received daratumumab 4 mg/kg on Day 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants received daratumumab 16 mg/kg on Days 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants received daratumumab 16 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Reporting group title	Phase 1: 8mg/kg Daratumumab + Lenalidomide and Dexamethasone

Reporting group description:

Participants received with daratumumab 8 mg/kg on Days 0 (pre dose infusion), 1, 8, 15, 22 (cycle 1), Days 1, 8, 15, and 22 (cycle 2), Days 1 and 15 (cycles 3 to 6), Day 1 (cycle 7+) along with lenalidomide 25 mg on Day 1 to 21 of each 28-day cycle and dexamethasone 40 mg (weekly) and may be reduced to 20 mg (weekly after cycle 6 at the investigator's discretion). Each treatment cycle consists of 28 days.

Serious adverse events	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	22 / 32 (68.75%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma Gastric			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr Virus Associated Lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden Death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Laryngeal Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary Embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Influenza A Virus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Spinal Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic Fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle Fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral Infarction			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal Artery Thrombosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Steroid Withdrawal Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Viral Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8mg/kg Daratumumab + Lenalidomide and Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma Gastric			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr Virus Associated Lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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			
Sudden Death			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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			
Laryngeal Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Influenza A Virus Test Positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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			
Spinal Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral Infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal Artery Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Steroid Withdrawal Syndrome			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Viral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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 / 3 (0.00%)	0 / 4 (0.00%)	
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	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
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	Phase 1: 2 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 4 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 2: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	31 / 32 (96.88%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	10 / 32 (31.25%)
occurrences (all)	0	0	12

Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	5
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	13 / 32 (40.63%)
occurrences (all)	3	1	19
Application Site Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	0	0	7
Chest Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Facial Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	3 / 32 (9.38%)
occurrences (all)	2	1	3
Oedema Peripheral			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	8 / 32 (25.00%)
occurrences (all)	3	0	9
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Peripheral Swelling			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	9 / 32 (28.13%)
occurrences (all)	1	1	12
Influenza Like Illness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	4 / 32 (12.50%)
occurrences (all)	0	2	7
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Immune System Disorder			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Productive Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Oropharyngeal Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	3
Nasal Congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	1	4
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Dyspnoea Exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	4
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	4
Dry Throat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	16 / 32 (50.00%)
occurrences (all)	0	2	30
Bronchospasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Allergic Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Rhinitis Allergic			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	4 / 32 (12.50%)
occurrences (all)	0	3	4
Sputum Discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Mood Altered			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	8 / 32 (25.00%)
occurrences (all)	1	2	11
Disinhibition			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Depressed Mood			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	7
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	3
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	3 / 32 (9.38%)
occurrences (all)	0	2	4
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Blood Iron Decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	2
Blood Phosphorus Decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Blood Pressure Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3

Weight Decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 32 (9.38%)
occurrences (all)	0	1	3
C-Reactive Protein Increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Creatinine Renal Clearance Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Electrocardiogram QT Prolonged			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	3	0	7
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Clavicle Fracture			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Limb Injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Pelvic Fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	2	0	1
Palpitations			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Supraventricular Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences (all)	1	1	2
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Post Herpetic Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	2	2
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	7 / 32 (21.88%)
occurrences (all)	1	1	9
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	6 / 32 (18.75%)
occurrences (all)	2	2	9
Embolic Stroke			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	3
Dizziness Postural			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	4

Visual Field Defect			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	8 / 32 (25.00%)
occurrences (all)	0	3	26
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	8 / 32 (25.00%)
occurrences (all)	0	0	27
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	5 / 32 (15.63%)
occurrences (all)	0	1	8
Neutropenia			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	29 / 32 (90.63%)
occurrences (all)	8	3	114
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	11 / 32 (34.38%)
occurrences (all)	3	10	29
Ear and labyrinth disorders			
Hearing Impaired			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Lacrimation Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Retinal Artery Thrombosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	2	0	0
Vision Blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Visual Impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Vitreous Detachment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	3 / 32 (9.38%)
occurrences (all)	0	4	3
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Abdominal Discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Abdominal Pain Upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	0	0	6
Constipation			

subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	7 / 32 (21.88%)
occurrences (all)	3	4	13
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	18 / 32 (56.25%)
occurrences (all)	9	7	33
Dry Mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Faeces Discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	2
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Hypoaesthesia Oral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Mouth Ulceration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	11 / 32 (34.38%)
occurrences (all)	2	2	14
Toothache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	5 / 32 (15.63%)
occurrences (all)	0	1	6
Tongue Blistering			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	0	0	5
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Rash Generalised			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Dermal Cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Skin Disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Skin Fragility			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Skin Lesion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Skin Ulcer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Nocturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Renal Impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	5	1
Polyuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Urinary Retention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Pituitary-Dependent Cushing's Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Steroid Withdrawal Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Muscular Weakness			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	2	0	0
Muscle Spasms			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	15 / 32 (46.88%)
occurrences (all)	2	4	23
Joint Contracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Gouty Arthritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Bone Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	6 / 32 (18.75%)
occurrences (all)	1	2	9
Myopathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Musculoskeletal Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	5
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Back Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	8 / 32 (25.00%)
occurrences (all)	0	2	9
Neck Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Osteonecrosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pain in Jaw			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Pain in Extremity			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	1	0	5
Osteonecrosis of Jaw			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Diarrhoea Infectious			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	9 / 32 (28.13%)
occurrences (all)	0	0	14
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 32 (3.13%)
occurrences (all)	0	6	1
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Fungal Skin Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	3	0	5
Gastroenteritis Viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Herpes Zoster			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	3 / 32 (9.38%)
occurrences (all)	0	1	3
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	5
Oral Herpes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	1	3
Kidney Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	4	3	0
Lower Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Lung Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	10 / 32 (31.25%)
occurrences (all)	1	3	19
Oral Candidiasis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Influenza			

subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	3 / 32 (9.38%)
occurrences (all)	1	1	3
Oral Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 32 (12.50%)
occurrences (all)	0	0	4
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Postoperative Wound Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	8 / 32 (25.00%)
occurrences (all)	0	0	8
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 32 (3.13%)
occurrences (all)	2	0	1
Tooth Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	8 / 32 (25.00%)
occurrences (all)	3	9	16
Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	4
Viral Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 32 (6.25%)
occurrences (all)	0	2	2
Viral Upper Respiratory Tract			

Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	4 / 32 (12.50%)
occurrences (all)	3	2	4
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	4 / 32 (12.50%)
occurrences (all)	1	4	8
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	3
Decreased Appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3

Non-serious adverse events	Phase 1: 16 mg/kg Daratumumab + Lenalidomide and Dexamethasone	Phase 1: 8mg/kg Daratumumab + Lenalidomide and Dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 4 (100.00%)	

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	4 / 4 (100.00%)	
occurrences (all)	3	6	
Application Site Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	4	0	
Chest Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Facial Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	2	
Oedema Peripheral			
subjects affected / exposed	3 / 3 (100.00%)	1 / 4 (25.00%)	
occurrences (all)	4	2	
Pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peripheral Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Influenza Like Illness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Immune System Disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Productive Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nasal Congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Dyspnoea Exertional			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	
occurrences (all)	2	2	
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dry Throat			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	
occurrences (all)	1	7	
Bronchospasm			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Allergic Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Rhinitis Allergic			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Sputum Discoloured			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Mood Altered			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 4 (75.00%)	
occurrences (all)	0	3	

Disinhibition			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Depressed Mood			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood Iron Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood Phosphorus Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

Blood Pressure Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Weight Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
C-Reactive Protein Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Creatinine Renal Clearance Decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT Prolonged			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Clavicle Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Limb Injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pelvic Fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			

Atrial Fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Supraventricular Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Post Herpetic Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 3 (33.33%)	3 / 4 (75.00%)	
occurrences (all)	1	4	
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	2	
Embolic Stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dizziness Postural			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Visual Field Defect			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	4 / 4 (100.00%)	
occurrences (all)	8	13	
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	5	
Ear and labyrinth disorders			
Hearing Impaired			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Tinnitus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Lacrimation Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Retinal Artery Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vision Blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Visual Impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vitreous Detachment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Abdominal Discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Abdominal Pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Abdominal Pain Upper				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Constipation				
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)		
occurrences (all)	1	1		
Diarrhoea				
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)		
occurrences (all)	2	12		
Dry Mouth				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Faeces Discoloured				
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)		
occurrences (all)	1	0		
Gastrooesophageal Reflux Disease				
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)		
occurrences (all)	1	0		
Haemorrhoids				
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)		
occurrences (all)	0	1		
Hypoaesthesia Oral				
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)		
occurrences (all)	1	0		
Mouth Ulceration				
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)		
occurrences (all)	0	1		
Nausea				
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)		
occurrences (all)	1	4		
Toothache				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Vomiting				

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Tongue Blistering			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	2	
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Rash Generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dermal Cyst			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin Disorder			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Skin Fragility			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin Lesion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin Ulcer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nocturia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Renal Impairment			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Polyuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Urinary Retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Pituitary-Dependent Cushing's Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Steroid Withdrawal Syndrome			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	3	2	
Muscular Weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscle Spasms			
subjects affected / exposed	3 / 3 (100.00%)	3 / 4 (75.00%)	
occurrences (all)	3	5	
Joint Contracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Gouty Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Bone Pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	6	
Myopathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Musculoskeletal Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Musculoskeletal Chest Pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Back Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Neck Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Osteonecrosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pain in Jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pain in Extremity			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Osteonecrosis of Jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Diarrhoea Infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	2 / 3 (66.67%)	0 / 4 (0.00%)	
occurrences (all)	5	0	
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Cystitis				
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)		
occurrences (all)	2	0		
Erysipelas				
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)		
occurrences (all)	0	1		
Fungal Skin Infection				
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)		
occurrences (all)	0	1		
Gastroenteritis				
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)		
occurrences (all)	0	1		
Gastroenteritis Viral				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Herpes Zoster				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Infection				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Oral Herpes				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Kidney Infection				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Lower Respiratory Tract Infection				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Lower Respiratory Tract Infection Viral				
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)		
occurrences (all)	0	0		
Lung Infection				

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 3 (66.67%)	3 / 4 (75.00%)	
occurrences (all)	2	6	
Oral Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oral Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Postoperative Wound Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Urinary Tract Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	3	0	
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Tooth Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	3	
Respiratory Tract Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Viral Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal Mycotic Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	
occurrences (all)	1	2	
Decreased Appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2012	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
23 February 2012	The overall rationale for the amendment was to be nonsubstantial based on the criteria set forth in Article 10(a) of Directive 2001/20/European community (EC) of the European Parliament and the Council of the European Union, in that it does not significantly impact the safety or physical/mental integrity of subjects, nor the scientific value of the study.
26 July 2012	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
25 February 2013	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
26 February 2014	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
12 January 2015	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
06 October 2015	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.
29 September 2016	The overall rationale for the amendment was to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported