



Clinical trial results:

An Open-Label Treatment Use Protocol for Daratumumab in Subjects with Multiple Myeloma Who Have Received at Least 3 Prior Lines of Therapy (Including a Proteasome Inhibitor and an Immunomodulatory Agent) or are Double Refractory to a Proteasome Inhibitor and an Immunomodulatory Agent

Summary

EudraCT number	2015-002993-19
Trial protocol	GB ES IT
Global end of trial date	02 August 2018

Results information

Result version number	v1 (current)
This version publication date	22 August 2019
First version publication date	22 August 2019

Trial information

Trial identification

Sponsor protocol code	54767414MMY3010
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02477891
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	15 July 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to provide early access to daratumumab treatment and collect additional safety data while the medication was not yet commercially available for subjects with multiple myeloma who had received at least 3 prior lines of therapy including a proteasome inhibitor (PI) and an Immunomodulatory agent (IMiD) or whose disease was double refractory to both a PI and an IMiD.

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. Safety was evaluated based on the following variables: Adverse events, Clinical laboratory tests (hematology, serum chemistry, and urinalysis), Vital sign measurements, Physical examinations, and Eastern Cooperative Oncology Group (ECOG) performance status.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2015
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	Brazil: 49
Country: Number of subjects enrolled	Spain: 73
Country: Number of subjects enrolled	United Kingdom: 98
Country: Number of subjects enrolled	Italy: 72
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	United States: 348
Worldwide total number of subjects	692
EEA total number of subjects	243

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)	338
From 65 to 84 years	348
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 692 subjects were analyzed in this study.

Period 1

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

Arms

Arm title	DARATUMUMAB 16 mg/kg
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Arm description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion on Days 1, 8, 15, and 22 of Cycles 1 and 2 (weekly dosing), on Days 1 and 15 of Cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of Cycle 7 and subsequent cycles (every 4 weeks dosing) until disease progression, unacceptable toxicity, subject was no longer receiving clinical benefit, or the end of study. Each cycle was of 28 days.

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

Dosage and administration details:

Subjects received daratumumab 16 mg/kg on Days 1, 8, 15, and 22 of Cycles 1 and 2 (weekly dosing), on Days 1 and 15 of Cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of Cycle 7 and subsequent cycles (every 4 weeks dosing).

Number of subjects in period 1	DARATUMUMAB 16 mg/kg
Started	692
Completed	18
Not completed	674
Adverse event, serious fatal	38
Physician decision	7
Market authorization/reimbursement	231
Disease relapse	7
Adverse event	27
Adverse event - other	1
Consent withdrawn by subject	15
Non-compliance with study drug	1

Adverse event, serious non-fatal	1
Unspecified	7
Progressive disease	333
Lost to follow-up	4
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	DARATUMUMAB 16 mg/kg
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Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion on Days 1, 8, 15, and 22 of Cycles 1 and 2 (weekly dosing), on Days 1 and 15 of Cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of Cycle 7 and subsequent cycles (every 4 weeks dosing) until disease progression, unacceptable toxicity, subject was no longer receiving clinical benefit, or the end of study. Each cycle was of 28 days.

Reporting group values	DARATUMUMAB 16 mg/kg	Total	
Number of subjects	692	692	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	338	338	
From 65 to 84 years	348	348	
85 years and over	6	6	
Title for AgeContinuous Units: years			
arithmetic mean	64.2		
standard deviation	± 9.82	-	
Title for Gender Units: subjects			
Female	306	306	
Male	386	386	

End points

End points reporting groups

Reporting group title	DARATUMUMAB 16 mg/kg
Reporting group description:	
Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion on Days 1, 8, 15, and 22 of Cycles 1 and 2 (weekly dosing), on Days 1 and 15 of Cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of Cycle 7 and subsequent cycles (every 4 weeks dosing) until disease progression, unacceptable toxicity, subject was no longer receiving clinical benefit, or the end of study. Each cycle was of 28 days.	

Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs ^[1]
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End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non investigational) product and does not necessarily have a causal relationship with treatment. TEAEs are defined as any AE with onset date and time on or after that of first dose through 30 days after last study drug administration, or any AE that is considered related to (very likely, probably, or possibly related) study medication regardless of start date of event. Serious TEAEs was an AE that resulted in any of the following outcomes: death, life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, suspected transmission of any infectious agent via a medicinal product. All treated analysis population includes subjects who received at least one dose of study drug.

End point type	Primary
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End point timeframe:

Up to 3.1 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	DARATUMUMAB 16 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	692			
Units: Subjects				
TEAEs	561			
Serious TEAEs	283			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Grade 3 or 4 TEAEs

End point title	Number of Subjects With Grade 3 or 4 TEAEs ^[2]
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End point description:

TEAEs are defined as any AE with onset date and time on or after that of the first dose through 30 days after the last study drug administration, or any AE that is considered related to (very likely, probably, or

possibly related) study medication regardless of the start date of the event. Subjects with grade 3 or 4 TEAEs were assessed.

End point type	Primary
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End point timeframe:

Up to 3.1 years

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	DARATUMUMA B 16 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	692			
Units: Subjects	372			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3.1 Years

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	DARATUMUMAB
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Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion on Days 1, 8, 15, and 22 of Cycles 1 and 2 (weekly dosing), on Days 1 and 15 of Cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of Cycle 7 and subsequent cycles (every 4 weeks dosing) until disease progression, unacceptable toxicity, subject was no longer receiving clinical benefit, or the end of study. Each cycle was of 28 days.

Serious adverse events	DARATUMUMAB		
Total subjects affected by serious adverse events			
subjects affected / exposed	283 / 692 (40.90%)		
number of deaths (all causes)	60		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma Cell Leukaemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Plasma Cell Myeloma			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Plasmacytoma			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Squamous Cell Carcinoma of Skin			

subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial Stenosis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep Vein Thrombosis			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		
Hypertension			
subjects affected / exposed	7 / 692 (1.01%)		
occurrences causally related to treatment / all	5 / 7		
deaths causally related to treatment / all	0 / 0		
Lymphoedema			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	1 / 1		
Shock			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		

Chest Discomfort				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Chest Pain				
subjects affected / exposed	5 / 692 (0.72%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 2			
Chills				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Condition Aggravated				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Device Dislocation				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disease Progression				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Fatigue				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
General Physical Health Deterioration				
subjects affected / exposed	11 / 692 (1.59%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 10			
Infusion Site Reaction				

subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pain			
subjects affected / exposed	5 / 692 (0.72%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Non-Cardiac Chest Pain			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	23 / 692 (3.32%)		
occurrences causally related to treatment / all	9 / 25		
deaths causally related to treatment / all	1 / 2		
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Pelvic Pain			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	5 / 692 (0.72%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	13 / 692 (1.88%)		
occurrences causally related to treatment / all	6 / 14		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Lung Disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Obstructive Airways Disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Nasal Congestion				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural Effusion				
subjects affected / exposed	5 / 692 (0.72%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 1			
Pleural Fibrosis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleuritic Pain				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia Aspiration				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Embolism				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pulmonary Oedema				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Respiratory Failure				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Rhinorrhoea				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sneezing			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Throat Irritation			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Wheezing			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Throat Tightness			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional State			
subjects affected / exposed	7 / 692 (1.01%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 1		
Mental Status Changes			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Substance-Induced Psychotic Disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			

Blood Creatinine Increased subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General Physical Condition Abnormal subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ejection Fraction Decreased subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oxygen Saturation Decreased subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Femoral Neck Fracture subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur Fracture subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Fracture subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Infusion Related Reaction				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Hip Fracture				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Multiple Fractures				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic Fracture				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib Fracture				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Compression Fracture				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Cord Injury Thoracic				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Spinal Fracture				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Subdural Haematoma				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Sternal Fracture			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thoracic Vertebral Fracture			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper Limb Fracture			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Atrial Fibrillation			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Atrial Flutter			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 1		
Cardiac Failure Acute			

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac Failure Congestive			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiopulmonary Failure			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiovascular Insufficiency			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Left Ventricular Dysfunction			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Infarction			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Central Nervous System Lesion			

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cerebrovascular Accident				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cognitive Disorder				
subjects affected / exposed	3 / 692 (0.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic Stroke				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of Consciousness				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Posterior Reversible Encephalopathy Syndrome				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Speech Disorder				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Spinal Cord Compression			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Status Epilepticus			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Subarachnoid Haemorrhage			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient Ischaemic Attack			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vith Nerve Paralysis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	12 / 692 (1.73%)		
occurrences causally related to treatment / all	3 / 12		
deaths causally related to treatment / all	0 / 1		
Bone Marrow Failure			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Febrile Neutropenia			
subjects affected / exposed	13 / 692 (1.88%)		
occurrences causally related to treatment / all	3 / 13		
deaths causally related to treatment / all	1 / 2		
Hyperviscosity Syndrome			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 1		
Pancytopenia			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Thrombocytopenia			
subjects affected / exposed	18 / 692 (2.60%)		
occurrences causally related to treatment / all	7 / 29		
deaths causally related to treatment / all	0 / 1		
Ear and labyrinth disorders			
Ear Haemorrhage			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Eye Pruritus			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal Detachment			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	4 / 692 (0.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Perforation			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Oesophageal Ulcer			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oral Pruritus			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal Haemorrhage			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic Failure			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	14 / 692 (2.02%)		
occurrences causally related to treatment / all	2 / 14		
deaths causally related to treatment / all	0 / 3		
Chronic Kidney Disease			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cystitis Noninfective			

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Disorder			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	7 / 692 (1.01%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 3		
Renal Impairment			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Back Pain			
subjects affected / exposed	12 / 692 (1.73%)		
occurrences causally related to treatment / all	1 / 14		
deaths causally related to treatment / all	0 / 0		
Bone Pain			

subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Fracture Pain			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle Spasms			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular Weakness			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal Chest Pain			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteolysis			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pain in Extremity			
subjects affected / exposed	3 / 692 (0.43%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Pathological Fracture			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Pain			

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Adenovirus Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bacterial Sepsis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Campylobacter Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium Difficile Infection			

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia Bacteraemia				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia Sepsis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric Infection				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	5 / 692 (0.72%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster Disseminated				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower Respiratory Tract Infection			
subjects affected / exposed	11 / 692 (1.59%)		
occurrences causally related to treatment / all	5 / 12		
deaths causally related to treatment / all	0 / 1		
Lung Infection			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		
Neutropenic Sepsis			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Parainfluenzae Virus Infection			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumococcal Bacteraemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumococcal Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	31 / 692 (4.48%)		
occurrences causally related to treatment / all	12 / 34		
deaths causally related to treatment / all	0 / 1		
Pneumonia Bacterial			

subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia Haemophilus				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Streptococcal				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Post Procedural Infection				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Sepsis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory Syncytial Virus Infection				
subjects affected / exposed	2 / 692 (0.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				
subjects affected / exposed	7 / 692 (1.01%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Rhinitis				
subjects affected / exposed	1 / 692 (0.14%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rhinovirus Infection				

subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	10 / 692 (1.45%)		
occurrences causally related to treatment / all	4 / 10		
deaths causally related to treatment / all	1 / 2		
Septic Shock			
subjects affected / exposed	5 / 692 (0.72%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 3		
Sinusitis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft Tissue Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Bacteraemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 692 (0.87%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			

subjects affected / exposed	8 / 692 (1.16%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 1		
Viral Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Failure to Thrive			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypercalcaemia			
subjects affected / exposed	24 / 692 (3.47%)		
occurrences causally related to treatment / all	2 / 31		
deaths causally related to treatment / all	0 / 2		
Hyperkalaemia			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			

subjects affected / exposed	2 / 692 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 692 (0.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DARATUMUMAB		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	373 / 692 (53.90%)		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	89 / 692 (12.86%)		
occurrences (all)	145		
Lymphopenia			
subjects affected / exposed	47 / 692 (6.79%)		
occurrences (all)	70		
Neutropenia			
subjects affected / exposed	67 / 692 (9.68%)		
occurrences (all)	117		
Thrombocytopenia			
subjects affected / exposed	106 / 692 (15.32%)		
occurrences (all)	227		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	66 / 692 (9.54%)		
occurrences (all)	73		
Pyrexia			
subjects affected / exposed	49 / 692 (7.08%)		
occurrences (all)	51		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	44 / 692 (6.36%) 47		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Nasal Congestion subjects affected / exposed occurrences (all) Throat Irritation subjects affected / exposed occurrences (all)	77 / 692 (11.13%) 80 68 / 692 (9.83%) 71 47 / 692 (6.79%) 48 35 / 692 (5.06%) 36		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2014	The first amendment included following changes- addition of an exclusion criterion for subjects who had prior exposure to any anti-CD38 monoclonal antibody.
15 July 2015	The second amendment included following changes- addition of Exit Interviews, clarification of the administration of post-infusion treatment, and reduction in sample size.
12 October 2015	The third amendment included following changes- increase in the sample size to accommodate sites globally, adoption of the "End of Study definition" for enrollment and marketing authorization, modification of the term "Exit Interview" to "Subject Interview" and the addition of the PRO, European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ) Multiple Myeloma Module 20 (MY20) at selected sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Number of subjects enrolled refers to the number of patients treated in this study.
The "number of subjects completed / not-completed breakdown by reasons table" refers to subjects completed / discontinued the study.

Notes: