Clinical trial results:
An Open Label, Phase 2 Study to Evaluate Efficacy and Safety of Daratumumab in Relapsed or Refractory Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, and Follicular Lymphoma

Summary

EudraCT number	2014-005299-26
Trial protocol	BE NL
Global end of trial date	01 June 2017

Results information

Result version number	v1 (current)
This version publication date	13 June 2018
First version publication date	13 June 2018

Trial information

Trial identification

Sponsor protocol code	54767414LYM2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02413489
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	01 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives were to assess overall response rate (ORR), including complete response (CR) and partial response (PR), of daratumumab in subjects with non-Hodgkin’s lymphoma (NHL) and to evaluate association between ORR and CD38 expression level in order to determine a threshold for CD38 expression level in each NHL subtype, above which daratumumab activity is enhanced.

Protection of trial subjects:

Safety evaluations included adverse event monitoring, physical examinations, electrocardiogram (ECG) monitoring, clinical laboratory parameters (hematology, urinalysis and chemistry), vital sign measurements, and Eastern Cooperative Oncology Group (ECOG) performance status.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 September 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	Korea, Republic of: 6
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	36
EEA total number of subjects	15

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	18
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total 36 subjects were treated (15 subjects in the diffuse large B-cell lymphoma {DLBCL} cohort, 16 subjects in the follicular lymphoma {FL} cohort, and 5 subjects in the mantle cell lymphoma {MCL} cohort).

Period 1

Period 1 title	End of Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Diffuse Large B-cell Lymphoma (DLBCL)

Arm description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Arm type	Experimental
Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

Arm title	Follicular Lymphoma (FL)

Arm description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Arm type	Experimental
Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

Arm title	Mantle Cell Lymphoma (MCL)

Arm description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Arm type	Experimental

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

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

Number of subjects in period 1	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)
Started	15	16	5
Completed	0	0	0
Not completed	15	16	5
Consent withdrawn by subject	2	-	-
Death	11	3	4
Study terminated by sponsor	2	13	1

Baseline characteristics

Reporting groups	
Reporting group title	Diffuse Large B-cell Lymphoma (DLBCL)
Reporting group description:	
Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	
Reporting group title	Follicular Lymphoma (FL)
Reporting group description:	
Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	
Reporting group title	Mantle Cell Lymphoma (MCL)
Reporting group description:	
Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	

Reporting group values	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)
Number of subjects	15	16	5
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	9	4
From 65 to 84 years	10	7	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	66.7	62.3	59.8
standard deviation	± 11.88	± 9.77	± 6.69
Title for Gender Units: subjects			
Female	6	5	0
Male	9	11	5
CD38 expression value			
The expression levels of CD38 were used to do diagnosis of MCL, DLBCL, or FL and measurable disease.			
Units: Percentage of CD38 expression			
arithmetic mean	76.3	70.3	64
standard deviation	± 18.07	± 16.78	± 8.22

Reporting group values	Total		
Number of subjects	36		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	18		
From 65 to 84 years	18		

85 years and over	0		

Title for AgeContinuous Units: years arithmetic mean standard deviation	- -		
Title for Gender Units: subjects			
Female	11		
Male	25		
CD38 expression value			
The expression levels of CD38 were used to do diagnosis of MCL, DLBCL, or FL and measurable disease.			
Units: Percentage of CD38 expression arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Diffuse Large B-cell Lymphoma (DLBCL)
Reporting group description:	
Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	
Reporting group title	Follicular Lymphoma (FL)
Reporting group description:	
Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	
Reporting group title	Mantle Cell Lymphoma (MCL)
Reporting group description:	
Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]
End point description:	
ORR was defined as the percentage of subjects who achieved complete response (CR) or partial response (PR). As per Revised Response Criteria for Malignant Lymphoma, Lymph node measurements were taken from Computed Tomography (CT), CT portion of the Positron Emission Tomography/Computed Tomography (PET/CT), or Magnetic resonance imaging (MRI) scans where applicable. CR is defined as complete disappearance of all evidence of disease; PR as a > 50 % decrease in the sum of the products of the maximal perpendicular diameters of measured lesions (SPD) and no new sites. The analysis population was all subjects that were treated with daratumumab. Here "99999" indicates data was not estimable as no subjects had response.	
End point type	Primary
End point timeframe:	
After the first dose until disease progression, withdrawal of consent from study participation, or the end of study (approximately 1.9 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	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	16	5	
Units: Percentage of subjects				
number (confidence interval 95%)	6.7 (0.2 to 31.9)	12.5 (1.6 to 38.3)	0 (0 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of response was the duration from the date of the initial documentation of a response to the date of first documented evidence of progressive disease (PD). PD is defined as any new lesion >1.5 centimeter (cm) in any axis or >=50% increase in previously involved sites. The analysis population was all subjects that were treated with daratumumab and who achieved overall response There was insufficient data to perform Kaplan Meier analysis, therefore individual data for each evaluable subject was reported.

End point type	Secondary

End point timeframe:

Approximately 1.9 years

End point values	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	2	0[2]	
Units: Months				
number (not applicable)				
Subject 1	1.6	0.7		
Subject 2	0	7.4		

Notes:

[2] - None of subjects achieved response for this particular arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the duration from the date of the first daratumumab dose to the date of Progression or death, whichever comes first. The analysis population was all subjects that were treated with daratumumab.

End point type	Secondary

End point timeframe:

Approximately 1.9 years

End point values	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	16	5	
Units: Months				
number (confidence interval 95%)	1.2 (0.6 to 1.7)	3.3 (1.9 to 3.8)	1.3 (0.5 to 1.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival was defined as the duration from the date of the first daratumumab dose to the date of death. The analysis population was all subjects that were treated with daratumumab. Here "99999" upper limit of CI was not estimable due to less number of subjects with events and "99999" for MCL group indicates that Upper limit of CI could not be estimated due to less number of subjects analyzed.

End point type	Secondary

End point timeframe:

Approximately 1.9 years

End point values	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	16	5	
Units: Months				
number (confidence interval 95%)	4.9 (2.1 to 9.0)	17.2 (15.0 to 99999)	4.8 (1.7 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

Time to response was defined as the duration from the date of the first dose of daratumumab to the earliest date that a response (CR/PR) is first documented. The analysis population was all subjects that were treated with daratumumab and who achieved overall response There was insufficient data to perform Kaplan Meier analysis, therefore individual data for each evaluable subject was reported.

End point type	Secondary

End point timeframe:
Approximately 1.9 years

End point values	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	2	0[3]	
Units: Months				
number (not applicable)				
Subject 1	1.9	2.3		
Subject 2	0	1.9		

Notes:
[3] - None of subjects achieved response for this particular arm.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 1.9 years

Adverse event reporting additional description:

Analysis set included all subjects who received at least 1 dose of study treatment, and contributed any safety data after the start of study treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Diffuse Large B-cell Lymphoma (DLBCL)

Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Reporting group title	Follicular Lymphoma (FL)

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Reporting group title	Mantle Cell Lymphoma (MCL)

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

Serious adverse events	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)	6 / 16 (37.50%)	3 / 5 (60.00%)
number of deaths (all causes)	11	3	4
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse Large B-Cell Lymphoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (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
Injury, poisoning and procedural complications			
Spinal Fracture			

subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (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			
Febrile Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (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
Thrombocytopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (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
General disorders and administration site conditions			
General Physical Health Deterioration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	2 / 5 (40.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Lower			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (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
Renal and urinary disorders			
Acute Kidney Injury			

subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (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
Chronic Kidney Disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia Cytomegaloviral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (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

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

Non-serious adverse events	Diffuse Large B-cell Lymphoma (DLBCL)	Follicular Lymphoma (FL)	Mantle Cell Lymphoma (MCL)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	16 / 16 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Hot Flush			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)	3 / 16 (18.75%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Catheter Site Erythema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Catheter Site Inflammation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Chest Discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	2 / 15 (13.33%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	2	1	1

Fatigue			
subjects affected / exposed	4 / 15 (26.67%)	3 / 16 (18.75%)	1 / 5 (20.00%)
occurrences (all)	4	4	1
General Physical Health Deterioration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Influenza Like Illness			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Malaise			
subjects affected / exposed	3 / 15 (20.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Oedema Peripheral			
subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	1 / 5 (20.00%)
occurrences (all)	1	2	3
Pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	2 / 15 (13.33%)	4 / 16 (25.00%)	1 / 5 (20.00%)
occurrences (all)	2	6	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 15 (46.67%)	6 / 16 (37.50%)	4 / 5 (80.00%)
occurrences (all)	7	9	5
Dysphonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	2 / 5 (40.00%)
occurrences (all)	1	2	3
Hiccups			

subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Laryngeal Oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal Congestion			
subjects affected / exposed	0 / 15 (0.00%)	3 / 16 (18.75%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Oropharyngeal Discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pharyngeal Oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pleural Effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Productive Cough			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Rales			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory Failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Sinus Congestion			

subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Throat Irritation			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	2 / 5 (40.00%)
occurrences (all)	0	2	3
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Delirium			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Depressed Mood			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 15 (20.00%)	2 / 16 (12.50%)	1 / 5 (20.00%)
occurrences (all)	3	3	1
Product issues			
Thrombosis in Device			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Aspartate Aminotransferase Increased			

subjects affected / exposed	2 / 15 (13.33%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
C-Reactive Protein Increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus Test Positive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Prostatic Specific Antigen Increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Weight Decreased			
subjects affected / exposed	3 / 15 (20.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
Weight Increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hip Fracture			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Procedural Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin Abrasion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Sinus Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Dysarthria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 15 (0.00%)	5 / 16 (31.25%)	1 / 5 (20.00%)
occurrences (all)	0	6	1
Nerve Compression			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Neuralgia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Post Herpetic Neuralgia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Sensory Disturbance			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	5 / 16 (31.25%)	1 / 5 (20.00%)
occurrences (all)	1	8	1
Leukopenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Lymph Node Pain			
subjects affected / exposed	2 / 15 (13.33%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Lymphadenopathy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lymphocytosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Neutropenia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	1	4	2
Thrombocytopenia			
subjects affected / exposed	3 / 15 (20.00%)	3 / 16 (18.75%)	1 / 5 (20.00%)
occurrences (all)	4	7	4
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Erythema of Eyelid			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eyelid Oedema			

subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Ocular Hyperaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Visual Acuity Reduced			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain			
subjects affected / exposed	2 / 15 (13.33%)	5 / 16 (31.25%)	1 / 5 (20.00%)
occurrences (all)	2	5	1
Abdominal Pain Lower			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Anal Incontinence			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	2 / 16 (12.50%)	1 / 5 (20.00%)
occurrences (all)	2	2	1
Dental Caries			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Dry Mouth			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	5 / 15 (33.33%)	1 / 16 (6.25%)	2 / 5 (40.00%)
occurrences (all)	7	1	3
Paraesthesia Oral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Swollen Tongue			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	4 / 15 (26.67%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	5	0	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood Blister			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Night Sweats			
subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Pain of Skin			

subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	3	3	0
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Skin Burning Sensation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	3 / 16 (18.75%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Renal and urinary disorders			
Chronic Kidney Disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Obstruction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urine Flow Decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Back Pain			
subjects affected / exposed	1 / 15 (6.67%)	4 / 16 (25.00%)	1 / 5 (20.00%)
occurrences (all)	2	5	1
Flank Pain			

subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Mobility Decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscle Spasms			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	2 / 5 (40.00%)
occurrences (all)	0	3	2
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Pain in Extremity			
subjects affected / exposed	0 / 15 (0.00%)	3 / 16 (18.75%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Pain in Jaw			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Peripheral Arthritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Fungal Skin Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Genital Herpes			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Groin Infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Herpes Zoster			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 16 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 15 (6.67%)	3 / 16 (18.75%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Urinary Tract Infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			

Decreased Appetite			
subjects affected / exposed	1 / 15 (6.67%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 16 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vitamin B12 Deficiency			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2015	The main reason of this amendment was to Optimization of candidate screening potential, elaboration on Indirect Antiglobulin (Coombs) Testing (IAT) during the Screening Phase due to the risk of daratumumab interference with IAT, as well as updates throughout the protocol to align with the other daratumumab protocols, and some minor editorial changes.

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.

The study was terminated due to 2 non-Hodgkin's lymphoma (NHL) subtypes ([DLBCL] and FL cohorts) meeting the futility criteria defined in the protocol, and the cell lymphoma (MCL) cohort not having adequate recruitment.

Notes: