Clinical trial results:
A Multicentre Open label Phase II study of Daratumumab in AL Amyloidosis
Patients not in VGPR or Better

Summary

EudraCT number	2016-000287-42
Trial protocol	FR IT
Global end of trial date	27 September 2019

Results information

Result version number	v1 (current)
This version publication date	27 February 2021
First version publication date	27 February 2021
Summary attachment (see zip file)	results (blood.pdf) Table1-Demographics and Baseline Characteristics (Table 1.pdf)

Trial information

Trial identification

Sponsor protocol code	I15015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02816476
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Limoges
Sponsor organisation address	2 Avenue Martin Luther King, LImoges, France, 87042
Public contact	Abdeslam BENTALEB, CHU de Limoges, 33 0555058616, drc@chu-limoges.fr
Scientific contact	Arnaud JACCARD, CHU de Limoges, +33 0555058637, arnaud.jaccard@chu-limoges.fr

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	02 December 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To Assess Overall Hematologic Response Rate (CR + VGPR) at the completion of 6 cycles of Daratumumab in patients with AL Amyloidosis not in CR or VGPR after any previous therapy

Protection of trial subjects:

The informed consent of a patient is obtained prior to any study related procedures as per Good Clinical Practices (GCP) as set forth in the ICH guidelines.
Documentation that informed consent occurred prior to the patient's entry into the study and of the informed consent process should be recorded in the patient's source documents. In addition, if a protocol is amended and it impacts on the content of the informed consent, patients participating in the study when the amended protocol isimplemented must be re-consented with the revised version of the informed consent.

The infusion is done under medical supervision and during hospitalization. Premedication and post medication are scheduled to avoid Infusion-related reactions. If infusion-related reactions occur, the infusion is paused/stoped

Finally, a DSMB was set up to monitor the progress of the trial and the adverse effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	12
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter, single-arm, open-label, phase II study was conducted at 14 Intergroupe Francophone du Myélome (IFM) centers and one center in Italy, and enrolled between September 2016 and April 2018

Pre-assignment

Screening details:

Patients with biopsy proven systemic AL and measurable disease with a difference between serum involved and uninvolved free light chain (dFLC) > 50 mg/l were included in this trial provided they were in relapse or did not reach Very Good Partial Response (VGPR: dFLC<40 mg/l) after the last therapy. Patients with concomitant symptomatic MM, bone mar

Period 1

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

Arms

Arm title	Treated patients
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment comprised six 4-week cycles of intravenous (IV) daratumumab (16 mg/kg) on days 1, 8, 15 and 22 for the first 2 cycles, then every other week for cycles 3-6

Number of subjects in period 1	Treated patients
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	Treated patients

Reporting group description: -

Reporting group values	Treated patients	Total	
Number of subjects	40	40	
Age categorical			
49 patients were screened, 40 patients were included and received at least 4 injections of daratumumab. Table 1 summarizes baseline patient and disease characteristics. Median age was 69 years (range, 45–83). Overall, 24 (60%) patients had cardiac involvement, 26 (65%) had renal involvement, and 26 (65%) had 2 or more organs involved. The median dFLC level at baseline was 164 mg/l (IQR, 112-334) and 16/40 had a dFLC>180 mg/l. Median NT-proBNP at baseline was 916 ng/L (IQR, 285-2302). Twenty-one (52.5%) patients had a creatinine clearance below 60 ml/min. Median time from			
Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	39	39	
Age continuous			
Units: years			
median	69		
standard deviation	± 2.87	-	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	25	25	

End points

End points reporting groups

Reporting group title	Treated patients

Reporting group description: -

Primary: VGPR or better at the completion of 6 daratumumab cycles

End point title	VGPR or better at the completion of 6 daratumumab cycles[1]

End point description:

End point type	Primary

End point timeframe:

After 6 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistics reported for single cohort.
No statistics for arms.

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Number of patients				
number (not applicable)	19			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to hematological response

End point title	Time to hematological response

End point description:

End point type	Secondary

End point timeframe:

at the completion of 6 cycles of Daratumumab

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Days				
number (not applicable)	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to best hematological response

End point title	Time to best hematological response

End point description:

End point type	Secondary

End point timeframe:

At six months

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: days				
number (not applicable)	28			

Statistical analyses

No statistical analyses for this end point

Secondary: Cardiac Response

End point title	Cardiac Response

End point description:

End point type	Secondary

End point timeframe:

At six months

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Number of patients				
number (not applicable)	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS),

End point title	Progression-free survival (PFS),

End point description:

End point type	Secondary

End point timeframe:

One year

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage	68			

Statistical analyses

No statistical analyses for this end point

Secondary: overall survival (OS).

End point title	overall survival (OS).

End point description:

End point type	Secondary

End point timeframe:

At one year

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage	90			

Statistical analyses

No statistical analyses for this end point

Secondary: Renal Response

End point title	Renal Response

End point description:

End point type	Secondary

End point timeframe:

At six months

End point values	Treated patients			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Number of patients				
number (not applicable)	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Until 30 days after the last dose of study drug, except for secondary malignancies (all throughout the study).

Adverse event reporting additional description:

Toxicities were graded according to National Cancer Institute Common Toxicity Criteria of Adverse Events (version 4.0; Bethesda, MD).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Treated patients

Reporting group description: -

Serious adverse events	Treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 40 (20.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			

Cardiac pacemaker insertion			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ruptured cerebral aneurysm			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 40 (72.50%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Hypotension			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Orthostatic hypotension			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	10		
Chest pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Fever			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Oedema			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	10		
Inflammation			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Chills			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	8		
Dyspnoea			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	6		
Rhinorrhoea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Congenital, familial and genetic disorders			
Macroglossia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Neuropathy peripheral			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Eye disorders			

Conjunctival haemorrhage subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 9 / 40 (22.50%) 11 6 / 40 (15.00%) 6 5 / 40 (12.50%) 5 4 / 40 (10.00%) 4 3 / 40 (7.50%) 3		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2		
Musculoskeletal and connective tissue disorders Bone pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 3 2 / 40 (5.00%) 2		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Pneumonia	 9 / 40 (22.50%) 9 		

subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Skin infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Hyperkalaemia Iron deficiency			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32108228