Clinical trial results:
PHASE III, MULTI-CENTER, RANDOMIZED, 48 WEEKS, DOUBLE-BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED STUDY TO EVALUATE EFFICACY AND SAFETY OF CER-001 ON VESSEL WALL AREA IN PATIENTS WITH GENETICALLY DEFINED FAMILIAL PRIMARY HYPOALPHALIPOPROTEINEMIA AND RECEIVING BACKGROUND OPTIMIZED LIPID THERAPY, WITH OPTIONAL OPEN-LABEL SAFETY EXTENSION

Summary

EudraCT number	2015-003713-23
Trial protocol	NL BE FR
Global end of trial date	21 December 2018

Results information

Result version number	v1 (current)
This version publication date	28 December 2019
First version publication date	28 December 2019
Summary attachment (see zip file)	TANGO study CSR synopsis (TANGO_CSR_Synopsis_V1.0_2019_12_05.pdf)

Trial information

Trial identification

Sponsor protocol code	CER-001-CLIN-009

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CERENIS THERAPEUTICS SA
Sponsor organisation address	33-43 Avenue Georges Pompidou, BALMA, France, 31130
Public contact	Mrs Constance KEYSERLING, CERENIS THERAPEUTICS, 0033 673045380, cpeyrottes@abionyx.com
Scientific contact	Mrs Constance KEYSERLING, CERENIS THERAPEUTICS, 0033 673045380, cpeyrottes@abionyx.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	26 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2018
Global end of trial reached?	Yes
Global end of trial date	21 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of 24 weeks treatment with CER-001 on carotid Mean Vessel Wall Area (MVWA) as compared to placebo using 3T magnetic resonance imaging (3T-MRI);
To evaluate the safety and tolerability of CER-001 administered for 24 weeks

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 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	Netherlands: 19
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	53
EEA total number of subjects	36

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)	52
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

53 patients had to be screened to randomize 30 patients.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	NaCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.9% Sodium Chloride Injection, USP (or equivalent ex-US) labelled and distributed by Catalent.

Arm title	CER-001

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CER-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Based on patient weight at Screening (8 mg/mL), using sodium chloride 0.9% injection, diluted all doses to an uniform administration volume of 250 mL.

Number of subjects in period 1[1]	Placebo	CER-001
Started	10	20
Completed	9	13
Not completed	1	7
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	4

Sponsor decision, lack of efficacy	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 53 patients were screened and only 30 were randomized due to screen Failure.

Baseline characteristics

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	CER-001
Reporting group description: -	

Primary: Change from baseline in carotid artery mean vessel wall area at 24 weeks

End point title	Change from baseline in carotid artery mean vessel wall area at 24 weeks[1]
End point description:	
End point type	Primary
End point timeframe:	
24 weeks	

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: A linear mixed-effect model was used for the analysis of this primary outcome. Nevertheless, despite a tendency regarding W24 visit and CER-001 treatment, no significant association was evidenced regarding the effect of CER-001 on carotid artery MVWA within 24 weeks of treatment (parameter estimate = -1.46; P-value = 0.051).

End point values	Placebo	CER-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	17		
Units: mm²				
arithmetic mean (standard deviation)	-0.23 (± 1.36)	0.33 (± 1.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline MVWA in the carotid artery at 8 weeks

End point title	Change from baseline MVWA in the carotid artery at 8 weeks
End point description:	
End point type	Secondary
End point timeframe:	
8 weeks	

End point values	Placebo	CER-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	16		
Units: mm²				
arithmetic mean (standard deviation)	-0.72 (± 1.74)	0.25 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline MVWA in the carotid at 48 weeks

End point title	Change from baseline MVWA in the carotid at 48 weeks

End point description:

End point type	Secondary

End point timeframe:

48 weeks

End point values	Placebo	CER-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	15		
Units: mm²				
arithmetic mean (standard deviation)	0.11 (± 1.99)	0.05 (± 1.22)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All observed or volunteered adverse events occurring during the study period, at any time from the signature of the informed consent until the final study evaluation, regardless of treatment group or suspected causal relationship to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Details are provided on the attached CSR synopsis

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2015	• Changes in the study phase from II/III to phase III • Clarification of the study objective by deleting the efficacy and safety evaluation of cer-001 on ApoA 1 • Update of the study methodology by adding clarification to the genetically defined familial primary hypoalphalipoproteinemia : FPHA – mutation in ApoA1 and/or ABCA1 gene, • Update of number of patients and the sample size calculation with a total of 30 patients instead of approximately 30 patients, • Modifications of study population • Update of the section 5 Risk Benefit Statement, since the contrast agent use was not requested for the MRIs in this study, • Update of the section 6.1 – overview of the study design and dose regimen selection, with addition of a time window of +/- 2 days around the strict weekly or biweekly date, • Update of the section 6.4 – Number of patients and assignment to treatment group, for clarification, • Minor modifications / clarifications of study procedures and the flowchart, • Update of the Section 8.5.1 - Assessment of Vascular Structure of the Carotid and Femoral with 3T-MRI with addition of a time window of +/- 7 days around the strict date, • Update of Section 8.6 – Assessments and Procedures for Patients who Prematurely Discontinue Study Medication, by deleting the following condition: "In case of stopping prematurely study medication because of positive testing for anti-ApoA-1 antibody, patient should also to come back monthly for testing until the anti-ApoA-1 antibodies level returns to screening value", • Update of the Section 8.7.5 – Immunogenicity Testing by clarification that in case of positive result for the presence of neutralizing anti-ApoA-1 antibody at the end of treatment period visit, the patients must return monthly for testing until the antibodies return to screening value, • Update of the Section 12.5 - Populations for Analysis, by modifiying the ITT population into midfied mITT population
13 December 2016	• Addition of an open-labeled safety extension phase after the 48 weeks of blinded treatment as described in the protocol version 2.0 19NOV2015, • Update of the planned recruitment period and anticipated study duration, • Update of the objectives and parameters related to open-labeled safety extension study, • Redefinition of study population with the update of ApoA-1 level as ≤110 mg/dL and HDL level as ≤ 35 mg/dL or 0.9 mmol/L, • Clarification to the inclusion criterion n°6 regarding the stable lipid lowering therapies definition • Addition of inclusion criteria for background symptomatic or asymptomatic cardiovascular disease, ApoA-1 level ≤ 110 mg/dL and HDL-cholesterol level ≤ 35 mg/dL or 0.9 mmol/L

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

21 December 2018	Results from the double-blind portion of the TANGO STUDY were analyzed and showed that although no major treatment-related adverse events were observed, confirming the safety and good tolerance profile of CER-001, there was also no evidence of benefit since analysis of the primary efficacy Endpoint data did not show a statistically significant reduction in carotid atheroma plaque of CER-001 relative to placebo treatment. In view of this lack of benefit to patients, the trial was terminated early.	-

Notes:

Limitations and caveats

None reported