

**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: mm ² | | | | |
| 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: mm ² | | | | |
| 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: mm ² | | | | |
| 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 | <ul style="list-style-type: none">• 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 modifying the ITT population into midfied mITT population |
| 13 December 2016 | <ul style="list-style-type: none">• 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. | - |
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Notes:

Limitations and caveats

None reported