



Clinical trial results:

Proof-of-pharmacology clinical trial on a vaccine that elicits a protective humoral immune response against oxidized low density lipoprotein

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-005650-35 |
| Trial protocol | NL |
| Global end of trial date | 30 August 2017 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 13 December 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | CHDR1503 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Centre for Human Drug Research |
| Sponsor organisation address | Zernikedreef 8, Leiden, Netherlands, 2333CL |
| Public contact | J. Burggraaf, Centre for Human Drug Research, +31 715246400, kb@chdr.nl |
| Scientific contact | J. Burggraaf, Centre for Human Drug Research, +31 715246400, kb@chdr.nl |

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 | 05 March 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 August 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 August 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To determine the specific immunoglobulin response against oxLDL after administration of a single 13-valent pneumococcal vaccine.

Protection of trial subjects:

The 13-valent pneumococcal vaccine consists of wall saccharides and thus no living organisms. Previous research has demonstrated that administration of the vaccine is safe, illustrated by its widespread implementation in clinical use in both infants and adults. Side effects are usually limited to local mild tenderness and, more infrequently, low grade fever (<39 C) or fatigue. Due to the extensive experience with the vaccine, we expect the risk of unexpected SAEs to be low. In terms of benefits, subjects may have a reduction in risk of developing pneumonia, although studies have predominantly been performed in the elderly or infants, thus no adequate estimation of risk reduction can be performed in the subjects of this study. Furthermore, this study may be the next step to show that the 13- valent conjugate vaccine may provide a safe and widely applicable treatment modality for atherosclerosis.

Written informed consent was obtained from each individual participating in the study prior to any study procedure and after adequate explanation of the aims, methods, objectives, and potential hazards of the study. It was made clear to each subject that he or she was completely free to refuse to enter the study, or to withdraw from it at any time for any reason.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|---|---------------|
| Actual start date of recruitment | 05 April 2016 |
| 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: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 24 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

05 April 2016 - 30 August 2017

Pre-assignment

Screening details:

Subjects enrolled are male, aged 18-45 without evidence of any active or chronic disease following a medical history, a complete physical examination including vital signs, 12-lead ECG, haematology, blood chemistry and urinalysis. Able to participate and willing to give written informed consent and to comply with the study restrictions

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, Assessor |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | AAA treatment |

Arm description:

3 times active treatment

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Prevenar-13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |

Dosage and administration details:

0,5 mL Prevenar-13 at baseline, after 4 weeks and after 28 weeks.

| | |
|------------------|-------------------|
| Arm title | Placebo treatment |
|------------------|-------------------|

Arm description:

3 times placebo treatment

| | |
|--|----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | 0.9% saline solution |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |

Dosage and administration details:

0.5 mL 0.9% saline solution at baseline, after 4 weeks and after 28 weeks.

| | |
|------------------|---------------|
| Arm title | AAP treatment |
|------------------|---------------|

Arm description:

2 times active , 1 time placebo treatment

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|-------------------|
| Investigational medicinal product name | Prevenar-13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0,5 mL Prevenar-13 at baseline, after 4 weeks and after 28 weeks. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | Placebo |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0.5 mL 0.9% saline solution at baseline, after 4 weeks and after 28 weeks. | |
| Arm title | APP treatment |
| Arm description: | |
| 1 time active, 2 times placebo treatment | |
| Arm type | Active comparator |
| Investigational medicinal product name | Prevenar-13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0,5 mL Prevenar-13 at baseline, after 4 weeks and after 28 weeks. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0.5 mL 0.9% saline solution at baseline, after 4 weeks and after 28 weeks. | |
| Arm title | APA treatment |
| Arm description: | |
| 2 times active, 1 placebo | |
| Arm type | Active comparator |
| Investigational medicinal product name | Prevenar-13 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0,5 mL Prevenar-13 at baseline, after 4 weeks and after 28 weeks. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Injection |
| Dosage and administration details: | |
| 0.5 mL 0.9% saline solution at baseline, after 4 weeks and after 28 weeks. | |

| Number of subjects in period 1 | AAA treatment | Placebo treatment | AAP treatment |
|---------------------------------------|---------------|-------------------|---------------|
| Started | 4 | 8 | 4 |
| Completed | 4 | 8 | 3 |
| Not completed | 0 | 0 | 1 |
| Consent withdrawn by subject | - | - | 1 |

| Number of subjects in period 1 | APP treatment | APA treatment |
|---------------------------------------|---------------|---------------|
| Started | 4 | 4 |
| Completed | 4 | 4 |
| Not completed | 0 | 0 |
| Consent withdrawn by subject | - | - |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|--------------------------------|---------------|-------|--|
| Number of subjects | 24 | 24 | |
| Age categorical | | | |
| Healthy males aged 18-45 years | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 24 | 24 | |
| Gender categorical | | | |
| Healthy males aged 18-45 years | | | |
| Units: Subjects | | | |
| Male | 24 | 24 | |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | AAA treatment |
| Reporting group description: 3 times active treatment | |
| Reporting group title | Placebo treatment |
| Reporting group description: 3 times placebo treatment | |
| Reporting group title | AAP treatment |
| Reporting group description: 2 times active , 1 time placebo treatment | |
| Reporting group title | APP treatment |
| Reporting group description: 1 time active, 2 times placebo treatment | |
| Reporting group title | APA treatment |
| Reporting group description: 2 times active, 1 placebo | |

Primary: Anti-oxLDL IgG

| | |
|--|-------------------------------|
| End point title | Anti-oxLDL IgG ^[1] |
| End point description: Prevenar-induced anti-oxLDL IgG antibodies | |
| End point type | Primary |
| End point timeframe: Overall trial (Baseline up to EOS) | |
| 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: Please refer to uploaded charts for the corresponding endpoint and statistical analysis. Also for other primary endpoints.

| End point values | AAA treatment | Placebo treatment | AAP treatment | APP treatment |
|-----------------------------|-----------------|-------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 8 | 4 | 4 |
| Units: RLU/100ms | | | | |
| number (not applicable) | 4 | 8 | 4 | 4 |

| End point values | APA treatment | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 4 | | | |
| Units: RLU/100ms | | | | |
| number (not applicable) | 4 | | | |

| | |
|-----------------------------------|---|
| Attachments (see zip file) | CHDR1503_ CSR endpoints and analyses summary_v1.0 |
|-----------------------------------|---|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall trial

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Active treatment |
|-----------------------|------------------|

Reporting group description: -

| | |
|-----------------------|-------------------|
| Reporting group title | Placebo treatment |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events | Active treatment | Placebo treatment | |
|---|------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| Non-serious adverse events | Active treatment | Placebo treatment | |
|---|------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 16 (81.25%) | 3 / 20 (15.00%) | |
| Cardiac disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 20 (5.00%) | |
| occurrences (all) | 1 | 1 | |
| Disturbance in attention | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration | | | |

| | | | |
|------------------------------------|-----------------|----------------|--|
| site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 20 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Injection site discomfort | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 20 (5.00%) | |
| occurrences (all) | 2 | 1 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 20 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| liver enzymes increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |

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