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