Clinical trial results:
A study to characterize the humoral and cellular response following simultaneous immunization with a neo-antigen (KLH) and a recall antigen (tetanus) in healthy volunteers

Summary

EudraCT number	2017-000084-32
Trial protocol	NL
Global end of trial date	09 May 2017

Results information

Result version number	v1 (current)
This version publication date	15 June 2022
First version publication date	15 June 2022
Summary attachment (see zip file)	CHDR1701_CSR Synopsis_01Nov2017 (CHDR1701_CSR Synopsis_01Nov2017.pdf)

Trial information

Trial identification

Sponsor protocol code	CHDR1701

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, 2333 CL
Public contact	Research Director, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Research Director, Centre for Human Drug Research, +31 715246400, clintrials@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	01 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2017
Global end of trial reached?	Yes
Global end of trial date	09 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigation of the immune response following immunization with Immucothel/Alhydrogel with or without tetanus. Per efficacy endpoint, the following parameters will be explored:
(a) Response size;
(b) Inter-individual variability of the response;
(c) Time course of the response.
Moreover, for each efficacy endpoint, it will be confirmed that a simultaneous administration of tetanus toxoid does not interfere (or only minimally) with the KLH response. This is valuable information to support simultaneous KLH/tetanus toxoid immunizations in the future intervention trial targeting OX40/OX40L. The data generated in the current study will allow selection of the most robust readout measures for quantification of the Immucothel/Alhydrogel-induced immune response in the future OX40/OX40L study and allow for a power analysis of studies using this model.

Protection of trial subjects:

Immunization with KLH is not expected to yield any benefit for the participating subjects. Since all participating subjects have been immunized with tetanus toxoid(see in-and exclusion criteria), any tetanus toxoid immunization in this study should be considered a booster immunization. This means that the six subjects that will be immunized with the tetanus toxoid immunization will not need a booster immunization in the ten years after completing this study.
In terms of risks, all drugs that are used in the present study are widely used in the Netherlands, and, apart from temporary side effects associated with the administration of the drugs, it is unlikely to expect that the subjects will be at risk of unforeseen events. Furthermore, all study drug administrations will be done in the clinic under medical supervision, and the subjects remain in the clinic for at least 30 minutes to closely monitor any adverse signs. Therefore, the risks associated with study participation are considered minimal

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2017
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall trial (overall period).

Pre-assignment

Screening details:

Healthy male subjects, 18 to 45 years of age (inclusive). Body mass index (BMI) between 18 and 30 kg/m2, inclusive, and with a minimum bodyweight of 50 kg. Anti-tetanus toxoid antibody titer ≥0.1 IU/mL.

Period 1

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

Blinding implementation details:

This study was performed in a double-blind fashion. The investigator, study staff, subjects, sponsor, and monitor remained blinded to the treatment assignment until database lock. The IMPs and its matching placebo were indistinguishable and were packaged and administered in the same way.

Arms

Are arms mutually exclusive?	Yes
Arm title	immunisation treatments

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Tetanus toxoid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

The dose of tetanus toxoid that is also used in clinical practice for repeated immunisation in adults (>40 IU in 0.5 mL) was also used in this study.

Investigational medicinal product name	Immucothel®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Immucothel® was adsorbed into Alhydrogel®, In this study the administered dose of KLH was 0.1 mg adsorbed in 0.9 mg of Alhydrogel.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

The IMPs and its matching placebo were indistinguishable and were packaged and administered in the same way.

Number of subjects in period 1	immunisation treatments	Placebo
Started	12	3
Completed	12	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
Gender categorical Units: Subjects			
Male	15	15	

End points

End points reporting groups

Reporting group title	immunisation treatments
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: 12 IgM antibody titer against KLH

End point title	12 IgM antibody titer against KLH[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 7 until day 28	

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: For results see attached document.

End point values	immunisation treatments	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: days	12	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

A treatment-emergent adverse event (TEAE) was defined as an adverse event observed after starting administration of the specific treatment, and up to 5 days (96 hours) after study drug administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	immunisation treatments
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	immunisation treatments	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 3 (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	immunisation treatments	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)	3 / 3 (100.00%)	
Injury, poisoning and procedural complications			
drug administration error			
subjects affected / exposed	2 / 12 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Injection site haematoma			
subjects affected / exposed	3 / 12 (25.00%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 12 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Skin burning sensation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	

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