Clinical trial results:
A dermal inflammatory challenge study to evaluate complement activation in healthy volunteers

Summary

EudraCT number	2020-005595-35
Trial protocol	NL
Global end of trial date	23 April 2021

Results information

Result version number	v1 (current)
This version publication date	19 October 2022
First version publication date	19 October 2022
Summary attachment (see zip file)	M2. CHDR2036_Synopsis CSR_09Mar2022 (M2. CHDR2036_Synopsis CSR_09Mar2022.pdf)

Trial information

Trial identification

Sponsor protocol code	CHDR2036

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Toetsingonline: NL76227.056.20

Notes:

Sponsors

Sponsor organisation name	Centre for Human Drug Research
Sponsor organisation address	Zernikedreef 8, Leiden, Netherlands, 2333 CL
Public contact	M. Moerland, Centre for Human Drug Research, +31 715246400, clintrails@chdr.nl
Scientific contact	M. Moerland, Centre for Human Drug Research, +31 715246400, clintrails@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	02 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2021
Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate complement activation in skin after topical imiquimod challenge
- To evaluate complement activation in skin after local UV-B challenge

Protection of trial subjects:

Aldara / imiquimod
Possible skin reactions should be monitored carefully during treatment. Since psoriasis exacerbations due to imiquimod treatment have been described, psoriasis patients as well as patients with other autoimmune diseases and skin diseases are excluded to participate in this study to minimize potential risk(s). CHDR has run multiple topical imiquimod challenge studies over the last 3 years, without any safety concerns. Imiquimod exposure in this study will be within the normal therapeutic range, at a limited duration.

UV-B
UV irradiation from sunlight is associated with an increased incidence of skin cancer. UV irradiation contains a spectrum of wavelengths with UV-B being one of the risk factors for skin cancer. The UV-B wavelength range used in this study is the narrow band (NB) range 310-315nm, which is also used for phototherapy of skin conditions such as psoriasis. In general, UV-B phototherapy is a very safe treatment modality [Lee, 2005].
Participants with pre-existing risk factor for skin cancer will be excluded. As risk mitigation, participants with Fitzpatrick skin type IV, V or VI will be excluded. Dose of UV irradiation will be at 2 x MED. The potential occurrence of hyperpigmentation will be carefully monitored. Before study participation, study participants will be thoroughly informed of the potential risk of PIH at the UV irradiation sites.

Skin punch biopsies
Since complement deposition can only be assessed histologically, skin biopsies are indispensable in this study. Biopsies will be taken in a minimally invasive manner. Since the diameter is only 3 mm no stitching is necessary.
Study participants will have no health benefit.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	19 February 2021
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: 11

Worldwide total number of subjects	11
EEA total number of subjects	11

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)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

19-FEB-2021 to 18-MAR-2021, the Netherlands

Pre-assignment

Screening details:

Enrolled in this study were healthy male participants with Fitzpatrick skin type I-III

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Imiquimod

Arm description:

Two-part inflammatory challenge study in HV.
Part 1: Imiquimod challenged group

Arm type	Experimental
Investigational medicinal product name	Imiquimod/Aldara
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

A dosage of 5 mg imiquimod (100 mg Aldara®) per treatment site was applied, for 3 days

Arm title	Part 2: UV-B

Arm description:

Two-part inflammatory challenge study in HV.
Part 2: UV-B challenged group

Arm type	Experimental without IMP

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Part 1: Imiquimod	Part 2: UV-B
Started	5	6
Completed	5	5
Not completed	0	1
Physician decision	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Adults (18-64 years)	11	11	
Gender categorical Units: Subjects			
Male	11	11	

End points

End points reporting groups

Reporting group title	Part 1: Imiquimod
Reporting group description:	
Two-part inflammatory challenge study in HV. Part 1: Imiquimod challenged group	
Reporting group title	Part 2: UV-B
Reporting group description:	
Two-part inflammatory challenge study in HV. Part 2: UV-B challenged group	

Primary: Complement factors in skin biopsies following imiquimod challenge

End point title	Complement factors in skin biopsies following imiquimod challenge[1][2]
End point description:	
In naïve, unchallenged skin, trace or mild C3d staining was observed in the dermis, with no significant C3c deposition. No significant induction of C3c was seen at any time point after imiquimod challenge.	
End point type	Primary
End point timeframe:	
Biopsies taken at baseline, 24h, 48hr, 72hr and 120hr post-dose.	

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: See attachment.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: See attachment.

End point values	Part 1: Imiquimod			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Intensity of staining signal				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Primary: Complement factors in skin biopsies following UV-B challenge

End point title	Complement factors in skin biopsies following UV-B
End point description:	
In naïve, unchallenged skin, trace or mild C3d staining was observed in the dermis, with no significant C3c deposition. No significant induction of C3c was seen at any time point after UV-B challenge.	
End point type	Primary

End point timeframe:

Biopsies taken at baseline, 6h, 24h, 48hr and 72hr post-UV-B challenge.

Notes:

[3] - 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: See attachment.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: See attachment.

End point values	Part 2: UV-B			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: IHC-staining				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Study day 1-8	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1
Reporting groups	
Reporting group title	Part 1: Imiquimod
Reporting group description: Two-part inflammatory challenge study in HV. Part 1: Imiquimod challenged group	
Reporting group title	Part 2: UV-B
Reporting group description: Two-part inflammatory challenge study in HV. Part 2: UV-B challenged group	

Serious adverse events	Part 1: Imiquimod	Part 2: UV-B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (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	Part 1: Imiquimod	Part 2: UV-B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	1 / 6 (16.67%)	
Injury, poisoning and procedural complications			
Application site pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 3	0 / 6 (0.00%) 0	
Skin and subcutaneous tissue disorders Skin lesion inflammation subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 6 (0.00%) 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