



Clinical trial results:

Assessment of Neublabin-Induced Skin and Sensory Alterations and Headache in Healthy Subjects and Migraine Patients

Summary

EudraCT number	2019-001771-36
Trial protocol	NL
Global end of trial date	30 September 2020

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022
Summary attachment (see zip file)	Summary of M2. CHDR1755_CSR (Summary of M2. CHDR1755_CSR.pdf)

Trial information

Trial identification

Sponsor protocol code	CHDR1755
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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	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Principal Investigator, 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	30 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2020
Global end of trial reached?	Yes
Global end of trial date	30 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objectives

1. To assess pruritus and rash after administration of Neublastin or placebo in healthy subjects and migraine patients (Parts A and B)
2. To assess headache and other migraine-associated symptoms after administration of Neublastin or placebo in migraine patients (Part B)

Protection of trial subjects:

To protect trial participants, the following safety measures were taken. Pre-dose and regular post-dose measurement of: - Adverse events

- Vital signs (pulse rate, blood pressure, respiration rate)
- Body temperature
- ECG
- Hematology blood sample
- Chemistry blood sample
- Urinalysis

Background therapy:

Migraine treatment NSAIDS and/or triptans (Part B)

Evidence for comparator:

A double-blinded and placebo-controlled design was deemed appropriate because of the pharmacodynamic assessments that were performed in this study. By blinding the study, bias arising from investigator's knowledge about treatment assignment on interpretation of the data was avoided.

Actual start date of recruitment	16 August 2019
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: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

Notes:

Subjects enrolled per age group

In utero	0
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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)	48
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment from July 2019- July 2020. Location: Netherlands

Pre-assignment

Screening details:

Healthy male or female subjects, 18-65 years of age (inclusive), without evidence of any active or chronic illness or any clinically significant abnormalities in laboratory test results, ECG and blood pressure.

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, Assessor

Blinding implementation details:

The investigational drug and the matching placebo were visually indistinguishable and were packaged and administered in the same way. Treatment and placebo were labelled with the subject's randomization number only.

Arms

Arm title	Neublastin treatment
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Arm description:

Part A (n=36)

- Cohort 1 (n=24): single intravenous administration of 150 µg/kg Neublastin (n=12) or placebo (n=12).
- Cohort 2 (n=12): single intradermal administration of 5 µg (n=3), 20 µg (n=3) or 100 µg (n=6) Neublastin in the left or right leg and matching placebo in the opposite leg. All subjects in cohort 2 also received an ID dose of Neublastin in the flank or upper back area.

Part B (n=12)

- Single intravenous administration of 50 µg/kg (n=6) or 150 µg/kg (n=6) Neublastin and matching placebo.

Arm type	Active comparator
Investigational medicinal product name	Neublasting
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intradermal use, Intravenous use

Dosage and administration details:

1.6 mg/ml solution for both IV infusion and ID injection.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intradermal use, Intravenous use

Dosage and administration details:

0.9% sodium chloride solution.

Number of subjects in period 1	Neublastin treatment
Started	48
Completed	48

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	48	48	
Age categorical			
Units: Subjects			
Adults (18-64 years)	48	48	
Gender categorical			
Units: Subjects			
Female	33	33	
Male	15	15	

End points

End points reporting groups

Reporting group title	Neublastin treatment
Reporting group description:	
Part A (n=36)	
- Cohort 1 (n=24): single intravenous administration of 150 µg/kg Neublastin (n=12) or placebo (n=12). - Cohort 2 (n=12): single intradermal administration of 5 µg (n=3), 20 µg (n=3) or 100 µg (n=6) Neublastin in the left or right leg and matching placebo in the opposite leg. All subjects in cohort 2 also received an ID dose of Neublastin in the flank or upper back area.	
Part B (n=12)	
Single intravenous administration of 50 µg/kg (n=6) or 150 µg/kg (n=6) Neublastin and matching placebo.	

Primary: Assessment of pruritus and rash (Part A and B) and headache (Part B)

End point title	Assessment of pruritus and rash (Part A and B) and headache (Part B) ^[1]
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End point description:

Part A and B:

- The assessment of pruritus (incidence, intensity, severity and duration) in healthy subjects and migraine patients over a 28-day period after challenge with Neublastin or placebo (ID and IV) as measured by the Pruritus Assessment questionnaire and 5-D Pruritus Scale questionnaire.
- The assessment of rash (incidence, area and severity, and qualitative assessments) in healthy subjects and migraine patients over a 28-day period after challenge with Neublastin or placebo (ID and IV) as measured by the Rash Assessment questionnaire, Eczema Area and Severity Index (EASI), patient-reported SCORing Atopic Dermatitis (PO-SCORAD) score, Erythema index and digital photography of rash.

Part B:

- The assessment of headache (incidence, severity, duration and incidence of migraine-associated symptoms) in migraine patients over a 28-day period after challenge with Neublastin or placebo (IV) as measured by the Headache Assessment questionnaire.

End point type	Primary
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End point timeframe:

28-day period

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 endpoints and analyses see attached CSR summary.

End point values	Neublastin treatment			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: questionnaire	48			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening (up to 28 days before dosing) until follow-up visits Day 28 (Part A) and Day 56 (Part B)

Adverse event reporting additional description:

Adverse events were investigated by the investigator routinely on all study visits and AE intensity, relationship to study intervention, chronicity and eventual actions related to the AE were determined.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Neublastin treatment
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Reporting group description:

Part A (n=36)

- Cohort 1 (n=24): single intravenous administration of 150 µg/kg Neublastin (n=12) or placebo (n=12).
- Cohort 2 (n=12): single intradermal administration of 5 µg (n=3), 20 µg (n=3) or 100 µg (n=6) Neublastin in the left or right leg and matching placebo in the opposite leg. All subjects in cohort 2 also received an ID dose of Neublastin in the flank or upper back area.

Part B (n=12)

- Single intravenous administration of 50 µg/kg (n=6) or 150 µg/kg (n=6) Neublastin and matching placebo.

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Neublastin treatment	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax spontaneous			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Neublabin treatment	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 48 (50.00%)	12 / 48 (25.00%)	
Nervous system disorders			
headache			
subjects affected / exposed	14 / 48 (29.17%)	12 / 48 (25.00%)	
occurrences (all)	17	15	
Migraine			
subjects affected / exposed	7 / 48 (14.58%)	9 / 48 (18.75%)	
occurrences (all)	18	11	
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	6 / 48 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	6	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 48 (4.17%)	0 / 48 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	14 / 48 (29.17%)	0 / 48 (0.00%)	
occurrences (all)	21	0	
Rash pruritic			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	14 / 48 (29.17%)	0 / 48 (0.00%)	
occurrences (all)	17	0	
rash			
subjects affected / exposed	3 / 48 (6.25%)	0 / 48 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2019	Change of dose.
24 December 2019	Change of dose.
16 June 2020	Restart of clinical study activities related to the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 March 2020	Covid-19 pandemic.	26 June 2020

Notes:

Limitations and caveats

None reported