# Clinical trial results:
# Assessment of Neublastin-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 |

### 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 |

| | |
|---|---|
| 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 |

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 |

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 48 | 48 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 48 | 48 | |
| Gender categorical<br>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] |
|---|---|

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 |
|---|---|

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

No statistical analyses for this end point

## 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

### 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.

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

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** | Neublastin 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