Pharmacological effects on nerve excitability in healthy volunteers

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25429

Source
Nationaal Trial Register

Brief title
CHDR1834

Health condition

• Pain

Sponsors and support

Primary sponsor: • Centre for Human Drug Research, Leiden
Source(s) of monetary or material Support: • CHDR investigator initiated study

Intervention

Outcome measures

Primary outcome

Pharmacodynamic endpoints:
- Nerve excitability threshold endpoints

Secondary outcome

PainCart endpoints
- lntra-epidermal electrical stimulation endpoints
- Tolerability / safety endpoints
Exploratory endpoints
Pharmacokinetic analysis will only be performed if a relevant pharmacodynamic effect is observed. Data will be used for PK or
PK-PD modelling.

Study description

Background summary

Neuronal excitability is largely dependent on voltage-gated sodium and potassium channels. In this study, we will investigate the effects of two drugs that inhibit the sodium channels, namely mexiletine and lacosamide, on nerve excitability and evoked pain tests in healthy subjects.
Measurement of peripheral nerve excitability would be an interesting biomarker for the efficacy of current and new treatments that influence the nerves. ln this study we will validate nerve excitability threshold tracking, a measurement technique for neuronal excitability. The placebo-controlled mexiletine and lacosamide administration should inform us about the sensitivity of threshold tracking to sodium channel blockade and will serye as a benchmark for future studies with selective sodium channel
blockers. Additionally, the effect of sodium channel blockers on evoked pa¡n tests, namely the PainCart test battery and intra-epidermal
electrical stimulation (lES), will be investigated.

Study objective

In this study we will validate nerve excitability threshold tracking, a measurement technique for neuronal
excitability. The placebo-controlled mexiletine and lacosamide administration should inform us about the sensitivity
of threshold tracking to sodium channel blockade and will serve as a benchmark for future studies with selective
sodium channel blockers. Measurement of peripheral nerve excitability would be an interesting biomarker for the
efficacy of current and new treatments that influence nerve excitability.

Study design

• 3 identical study visits

Intervention

Lacosamide / Mexiletine

Contacts

Public
NA

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Eligibility criteria

Inclusion criteria

1. Signed informed consent prior to any study-mandated procedure
2. Healthy male subjects, 18 to 45 years of age, inclusive at screening.
3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive at screening and with a minimum weight of 50 kg. .
4. Has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the
study restrictions.
5. All subjects must practice effective contraception during the study and be willing and able to continue
contraception for at least 90 days after their last dose of study treatment.

Exclusion criteria

1. Evidence of any active or chronic disease or condition that could interfere with, or for which the treatment of which might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in theopinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). Subjects with pre-dose findings of clinically significant changes in electrolytes should be excluded. In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.
8. Participation in an investigational drug or device study within 3 months prior to first dosing, or for more than 4 times a year
17. Any current, clinically significant, known medical condition in particular any existing conditions that would affect sensitivity to cold (such as atherosclerosis, Raynaud’s disease, urticaria, hypothyroidism) or pain (disease that causes pain, hypesthesia, hyperalgesia, allodynia, paraesthesia, neuropathy, etc.).
18. Subjects indicating pain tests intolerable at screening or achieving tolerance at >80% of maximum input intensity for any pain test for cold, pressure and electrical tests.
19. History or presence of post-inflammatory hyperpigmentation.
20. Dark skin (Fitzpatrick skin type IV, V or VI), widespread acne, freckles, tattoos or scarring on the back.
22. History of trauma to the upper extremities or other orthopaedic conditions that, in the opinion of the
investigator, could affect the electrophysiological measurements.
23. History of (or symptoms indicating presence of) carpal tunnel syndrome.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	05-08-2019
Enrollment:	18
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	10-10-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7327
NTR-old	NTR7543
Other	Stichting BEBO : CHDR1834 / NL67037.056.18 / 2018-003154-24

Study results

Summary results
NA