A randomized, single-center, double-blind, placebo-controlled, 2-way cross-over, single oral administration trial to evaluate blood-borne biomarker candidates to predict NOP receptor activation using GRT6010 as NOP receptor agonist in healthy human subjects.

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Primair: To assess the change in the CD11b expression in leukocytes and in plasma concentrations of nociceptin after oral single dose administration of 12 mg GRT6010 compared to placeboSecundair:To assess the difference in area of the capsaicin-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Interventional

Summary

ID

NL-OMON37607

Source
ToetsingOnline

Brief title
Evaluation biomarker to predict NOP receptor activation using GRT6010

Condition

- Peripheral neuropathies

Synonym
neuropathic pain

Research involving
Human

Sponsors and support

Primary sponsor: Grunenthal
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Evaluation of Biomarkers, Neuropathic pain, NOP receptor activation

Outcome measures

Primary outcome

Leukocyte CD11b expression levels, plasma nociceptin concentrations

Secondary outcome

Safety

Pharmacokinetics

Pharmacodynamics

Tolerability

Study description

Background summary

GRT6010 is a new investigational compound that may eventually be used for the treatment of neuropathic pain, chronic pain resulting from an injury to the nervous system. GRT6010 activates a signaling structure (receptor) called *NOP receptor*, which is related to but different from opioid receptors (e.g., the receptor for morphine). Receptors are proteins found on the surface of a cell with the ability to react on body or foreign signaling molecules. GRT6010 activates opioid receptors as well, but to a lesser extent. GRT6010 is not registered as a drug but has been given to humans before.

Study objective

Primair:
To assess the change in the CD11b expression in leukocytes and in plasma concentrations of nociceptin after oral single dose administration of 12 mg GRT6010 compared to placebo

Secundair:
To assess the difference in area of the capsaicin-induced flare and in the skin blood flow within that area between treatments with GRT6010 or placebo.
To assess the difference in pain assessments (brush-induced allodynia, mechanical pain threshold, heat pain threshold, and current pain) between treatments with GRT6010 or placebo after generating a sort of neuropathic pain by an intradermal capsaicin injection.
To assess the safety and tolerability of GRT6010.
To assess the pharmacokinetics of GRT6010 (including the influence of human AGP levels on the pharmacokinetics of GRT6010).
To assess the change in expression levels of selected genes from whole-blood mRNA after oral single dose administration of 12 mg GRT6010 compared to placebo

Study design

This is a randomized, single-center, double-blind, placebo-controlled, 2-period, cross-over, single oral administration, Phase I translational trial in 24 healthy male subjects.

The study will consist of 2 periods, during each period subjects will receive GRT6010 or inactive formulation (placebo) as a single dose of 12 mg in the form of an oral solution of 2 mL. During the study subjects will once receive GRT 6010 and once placebo.

Procedures and assessments during the study:
Screening , follow-up and during study: demographics, body weight and height (including body mass index calculation),
medical history, drug and alcohol screen, cotinine test, blood sampling for serology (HBsAg, anti HCV and anti-HIV 1/2),
DNA test (CYP2D6 genotyping) clinical chemistry, hematology, clotting, assessment biomarkers (mRNA, plasma nociceptin concentrations and leukocyte CD11b expression levels), alpha-1 acid glycoprotein, and pharmacokinetics,
Heart trace (ECG*s), assessment of pain after capsaicin administration; adverse events

Intervention

The study will consist of 6 groups, each group will stay in the clinical research centre for 2 periods of 5 days (4 nights) each (Day -1 to 4 and Day 28

to 32).

During the study subjects will receive GRT6010 or inactive formulation (placebo) after a fasting period (no food or drinks) of at least 10 hours. Subjects will receive the study medication as an oral solution in a syringe which will be emptied in their mouth; after this they will have to drink 240 mL of water. One (1) hour after the intake of the study medication they will receive an additional 240 mL of water. During the study they will receive GRT 6010 once and placebo once. Whether a subject will receive GRT6010 or placebo in Period 1 or 2 will be determined by chance.
The subject, nor the investigator knows when GRT6010 and placebo will be dosed; we call this *the study is blinded*. However, information on the administration of study medication will be present in the clinical research facility, in sealed envelopes, which can be opened in case of emergency.
For each period fasting will continue until 4 hours after drug administration. Then subjects will receive a lunch. During fasting and after intake of the study medication subjects are allowed to drink water with the exception of 1 hour prior to until 1 hour after drug administration.

During the study subject will undergo a pain test for 3 times. This pain test will be performed by generating a sort of neuropathic pain by an intradermal capsaicin injection (100ug/10ul), the hot substance in chili peppers, into the skin of the anterior side of one of their forearms. At several timepoints after the injection the extent to which this pain stimulus leads to increased pain sensation will be assessed.

Study burden and risks

During the study several assessments will be conducted differing in extent and the nature of burden:

Blood draws via direct puncture or an indwelling canula: It is anticipated that for each period 1 time an indwelling canula will be used besides blood will be drawn by direct puncture of the vein. Possible side effects of an indwelling canula are pain, light bleeding, heamatoma, possibly an infection.

Heart trace (ECG's): During the entire investigation ECG*s will be made regularly.

Pain test: During the study 3 times a pain test will be performed by generating a sort of neuropathic pain by injecting capsaicin (10ug/100ul). Soon after the injection, an area with increased pain/flare sensation (an intense, burning pain) and allodynia (a painful response to a usually non-painful stimulus) will develop around the injection site, in addition, there will be redness of the skin. These symptoms may last for 12-24 hours.

Telemetry: heart trace (ECG), rhythm and oxygen in blood will be monitored

continuously from 0.5 hours before dosing until 24 hours after dosing.

In a previous study with healthy volunteers GR6010 was considered safe and well tolerated and no serious adverse effects have been observed.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy male subjects
18-45 yrs, inclusive
BMI: 18.0-30.0 kg/m2, inclusive
non- or moderate smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2012
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	05-04-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2012-000503-32-NL
CCMO	NL40207.056.12