Double blind, randomized, 2-way cross-over, placebo controlled study to evaluate the therapeutic and preventive effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain in the UVB sunburn model in healthy male subjects

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PrimaryTo assess the preventative effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain in the UVB sunburn model using HPTol upon multiple dosing of GLPG1205 versus placebo.SecondaryTo further assess the preventative effect...

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

Summary

ID

NL-OMON44450

Source
ToetsingOnline

Brief title
GLPG1205-CL-106 (CS0285)

Condition

- Peripheral neuropathies

Synonym
inflammation induced pain, nociceptive pain, sensitization induced pain

Research involving
Human

Sponsors and support

Primary sponsor: Galapagos NV
Source(s) of monetary or material Support: Galapagos NV

Intervention

Keyword: Cross-over, Preventive, Therapeutic, UVB

Outcome measures

Primary outcome

Primary Endpoints (preventative setting)

HPTol at Day=6 (24h post-UVB exposure)

Secondary outcome

Secondary Endpoints (preventative setting):

* HPTol at Day 6

* HPThr at Day 6

* CPT at Day 6

* MDT at Day 6

* MPT at Day 6

* HPTol, HPThr, CPT, MDT, MPT time profile

Secondary Endpoints (therapeutic setting):

* HPThr Day 1

* HPTol Day 1

* CPT Day 1

* MDT Day 1

* MPT Day 1

* HPTol, HPThr, CPT, MDT, MPT time profile

Study description

Background summary

In vivo pharmacology effects observed with GLPG1205 confirm a role for GPR84 in neuro-inflammatory biology and, more precisely, support its role in the pathogenesis of pain.

An early indication for GLPG1205 efficacy in man is desired and can facilitate further development of this potential new treatment for e.g. pain. Based on the pre-clinical pharmacology of GLPG1205, the UVB sunburn model is a good model for obtaining an early read out of GLPG1205 potential efficacy. This UVB sunburn model is a method, well described in literature and widely applied in healthy subjects. The UVB model is a human and animal experimental pain model of a local cutaneous hyperalgesia and inflammation. The model is widely used for assessing efficacy and mode-of-action of analgesic and anti-inflammatory drugs in clinical trials. The UVB model induces thermal and mechanical hyperalgesia (primary hyperalgesia) at the site of irradiation and occasionally in the surrounding areas (secondary hyperalgesia). The induced inflammatory process, tissue damage, and released cytokines cause a characteristic demarked area of erythema (neurogenic inflammation). The UVB model is in particular useful for pharmacological screening as it can help translating data from animals to humans. The UVB induced primary hyperalgesia develops after approx. 24 h and remains for more than 48 h making the model useful in pharmacological screening studies with repeated dosing or for compounds with long lasting action.

Quantitative sensory testing (QST) assesses characteristic sensory patterns in pain models. The QST battery assembles a comprehensive list of robust and validated short form tests representing measures of all relevant sub-modalities of the somatosensory system. In the applied model for this study, the test battery of QST consists of mechanical detection threshold (MDT), mechanical pain threshold (MPT), cold pain threshold (CPT) and heat pain threshold (HPT).

In the current study the effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain (thermal and mechanical hyperalgesia) will be investigated by applying the UVB sunburn model in healthy male subjects. GLPG1205 will be evaluated in a therapeutic (after UV burn) and preventive setting (before UV burn) and compared with placebo.

Study objective

Primary
To assess the preventative effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain in the UVB sunburn model using HPTol upon multiple dosing of GLPG1205 versus placebo.

Secondary
To further assess the preventative effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain in the UVB sunburn model using other QST testing upon multiple dosing of GLPG1205 versus placebo.
To assess the therapeutic effect of GLPG1205 on nociceptive and inflammation/sensitization induced pain in the UVB sunburn model upon dosing of GLPG1205 versus placebo.
To evaluate the safety and tolerability of GLPG1205 after multiple oral dosing.
To assess the pharmacokinetics of GLPG1205 after multiple oral dosing.

3.3. EXPLORATORY OBJECTIVE
To explore the effect of GLPG1205 on inflammatory gene expression in skin biopsies following exposure to UVB radiation.

Study design

This study will be conducted as a randomized, placebo controlled, double blind, 2-way cross-over, and multiple oral dose study.

The study will consist of a screening period, 2 treatment periods of 8 days each separated by a washout period of at least 3 weeks. A follow-up examination will be performed 21 days (±2 days) after the last dose of the second treatment period.

After assessing eligibility during a 3-week screening period, 20 subjects will participate in the study. In each period, subjects will come to the study center on the day before first administration (Day -1) of the study drug. Baseline assessments and (re*)confirmation of eligibility will be assessed on Day -1 of Period 1. Subjects will remain in the study center until finalization of Day 3 study procedures. On Day 4, an ambulatory visit will take place. On Day 5, subjects will come back to the study center and remain in the study center until finalization of Day 8 study procedures. On Day 10 a phone call will take place for a post skin biopsy review.

Subjects will be randomized to one of the treatment sequences (GLPG1205 or placebo in a 1:1 ratio) prior to dosing on Day 1 of Period 1. On Day 1 of each period, subjects will receive an oral dose of either GLPG1205 500 mg or placebo. On Days 2 to 7, subjects will receive an oral dose of either GLPG1205 100 mg or placebo.

Safety and tolerability will be assessed throughout the study by adverse event reporting, vital signs recording, ECG recordings, physical examination, and clinical safety laboratory assessments. Subjects will also be assessed by a follow-up examination 21 days (±2 days) after the last dose.

During the screening process, subjects will be assessed for the minimal erythema dose (MED) of UVB light on the upper part of the left leg. Subjects subsequently will be exposed to three times the minimal erythema dose (MED) of UVB light on an approximately 4 x 4 cm area on the upper part of the leg in the morning of Day -1 and Day 5 (on Day -1 right leg, on Day 5 left leg). The MDT, MPT, CPT and HPT for assessing the pharmacodynamic effects will be assessed as detailed in the study flow chart (see protocol).

UVB radiation on a second area of the upper part of the leg (different area than the area used for QST testing) will be performed on Day 5 of Period 2 for collection of a skin biopsy 25 hours after first QST testing on Day 6 of Period 2.
Pharmacokinetic samples will be collected throughout the study to confirm steady state and exposure to GLPG1205, as per study flow chart (see protocol).

Study burden and risks

The dose levels of the study drugs are based on the previous clinical trials that were conducted by the sponsor. The risk to health at the chosen dosage is limited but subjects may experience one of the in the ICF mentioned side-effects or symptoms not previously reported. The subjects health will be closely monitored during the study to minimize these risks. If the subjects experience any side effects, the research physician will treat these where necessary. If new information becomes available about the safety of the study drug, the subjects will be informed as soon as possible.

In total, subjects will be exposed on 5 moments to UVB-radiation on an area of the skin on the upper leg to determine the Minimal Erythema Dose (MED) and for further tests. The symptoms related to this can be compared to a (very) light sunburn. In Period 2 on Day 5 subjects will be exposed to UVB-radiation on two areas instead of one. The second area will be used to collect skin tissue. In addition, the sensitivity to mechanical pressure, pain, heat and cold will be tested. These tests can lead to some discomfort.

To investigate the effect the study drug on the inflammatory gene expression of the skin after UVB radiation, 2 skin tissue samples (both 4 mm in diameter) will be collected from the upper leg: one from skin exposed to UVB and one from skin not exposed to UVB. The possible side effects related to this procedure are: formation of scar tissue, bleeding, bruising, infection, inflammation, soreness, and mild localized pain. Local anesthesia is used during the procedure.

The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting, bleeding or an infection at the blood sampling site can occur.

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

1. Subject has signed the informed consent form prior to any study related activity.
2. Subject is a healthy male volunteer between 18 and 65 years) of age (inclusive) at the screening (inclusive).
3. Subject has a BMI * 18.0 kg/m2 and * 30.0 kg/m2 at the screening.
4. Subject is appropriate for the study in the judgment of the investigator, based on physical examination, 12-lead electrocardiogram (ECG), laboratory tests, and subject*s interview.
5. Subject has a high probability for compliance with and completion of the study.

6. Subject agrees that he will use a condom and that in addition to that he (and his female partner of child-bearing potential) will use a highly effective method of contraception and will not donate sperm from first dose administration to 12 weeks after the last dose administration
7. Subject is non-smoker or is a light smoker (up to 5 cigarettes a day) and has not used more than the equivalent of 5 cigarettes a day of nicotine-containing products for at least 6 months.
8. Subject has skin type 1 or 2 according to Fitzpatrick Skin Typing Test.

Exclusion criteria

1. Subject shows clinically significant abnormalities in physical examination, ECG or vital signs, according to the investigator*s judgment.
2. Subject has a history of clinically significant endocrine, gastrointestinal, cardiovascular, hematological, hepatic, immunological, renal, respiratory, genitourinary or major neurological (including stroke and chronic seizures) abnormalities or diseases.
3. History of malignancy in the last 5 years, except basal cell carcinoma of the skin that has been treated and with no evidence of recurrence.
4. Subject has been exposed to GLPG1205 before.
5. Known hypersensitivity to GLPG1205 or excipients of the formulation. History of significant allergic reaction to any drug, such as anaphylaxis requiring hospitalization.
6. Subject had major surgery, donated or lost 1 unit of blood or plasma (approximately 500 mL) within 6 weeks prior to the first intake of the study drug.
7. Subject has participated in another investigational trial within 90 days prior to the intake of the study drug of this study.
8. Subject has used any prescription drug or herbal medicine within 14 days, over-the-counter medications or vitamin supplements within 7 days prior to Day 1.

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-08-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo

Ethics review

Approved WMO Date:	10-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-08-2017
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	EUCTR2017-002768-42-NL
CCMO	NL62707.056.17