A single-center, open-label, single oral dose study to investigate the absorption, distribution, metabolism, and excretion (ADME) and pharmacokinetics of EMA401 after a single dose of [14C]EMA401 in healthy male subjects

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

Summary

ID

NL-OMON44485

Source
ToetsingOnline

Brief title
EMA401 human ADME study in healthy male subjects

Condition

- Peripheral neuropathies

Synonym
neuralgia, peripheral neuropathic pain

Research involving

Human

Sponsors and support

Primary sponsor: Novartis Pharma AG
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ADME, EMA401

Outcome measures

Primary outcome

- Excretion/ mass balance of [14C]-radioactivity in excreta (urine, feces) as percentage (%) of administered dose

- Cmax, Tmax, AUC, T1/2 and any other PK parameters as appropriate from the concentration vs. time data of 14C radioactivity (whole blood, plasma)

- Cmax, Tmax, T1/2, AUC, CL/F, Vz/F any other pharmacokinetic parameter as appropriate from concentration vs. time profiles of EMA401 and known metabolites, if applicable.

Secondary outcome

All safety and tolerability data (including vital signs, ECG parameters, clinical safety laboratory parameters, averse events reporting, physical examination) up until and including 14 days post-dose

Study description

Background summary

EMA401 is a new investigational compound that may eventually be used for the treatment of peripheral neuropathic pain (also called neuralgia). Peripheral neuropathic pain is a long lasting type of pain that may occur after damage to

the brain, spinal cord or peripheral nerves (the word *peripheral* refers to the long nerves reaching out to the arms and legs). This pain is characterized by abnormal pain sensations including burning, stabbing or piercing pains.

In previous studies, EMA401 has shown to decrease the pain intensity in patients with shingles pain (nerve pain caused by a herpes zoster virus infection) and in patients with pain due to chemotherapy. EMA401 is in development and is not registered as a drug but has been given to humans before

Study objective

The purpose of the study is to investigate how quickly and to what extent EMA401 is absorbed, distributed, metabolized (broken down) and eliminated from the body (this is called pharmacokinetics). EMA401 will be labeled with 14-Carbon (14C) and is thus radioactive (also called radiolabeled). In this way EMA401 can be traced in blood, urine and feces. It will also be investigated to what extent EMA401 is tolerated. In addition, the influence of genetic factors on the pharmacokinetics of EMA401 may be explored.

Study design

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Groningen (location Martiniziekenhuis) for 9 to 15 days (8 to 14 nights).

During the study the volunteer will receive radiolabeled EMA401 after an overnight fast (at least 10 hours no eating and drinking) as a capsule, together with a minimum of 240 milliliters and a maximum of 480 milliliters of water.

Intervention

The volunteer will receive a single dose of 100 mg radiolabeled EMA401 as an oral capsule.

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. In previous clinical studies, approximately 316 people have been treated with EMA401. EMA401 has been administered to healthy volunteers as a single dose of up to 2000 mg or as twice daily doses of up to 1600 mg/day for 7 days. Possible side effects that were observed in previous studies include allergic skin rashes, elevation in liver enzymes (liver abnormalities), and a decreased level of white blood cells (neutropenia). Although there is some basis of suspicion that these side effects may be associated with EMA401, such an association has not been confirmed. Mild to moderate nausea and diarrhea

were the most frequent side effects, which were mostly seen in doses higher than will be tested in this study.

For the current study the possible side effects of EMA401 include: nausea, upper respiratory tract infections, headache, dizziness and pre syncope (state of lightheadedness, muscle weakness, and feeling faint). However, you should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. With the dose used in this study no serious adverse effects are expected.

In this study radiolabeled EMA401 will be used. The amount of radioactivity in this dose will be approximately 3.7 MBq (MBq = megaBecquerel, this is a unit to express the amount of radioactivity in the study compound). The average environmental background radiation burden in The Netherlands is approximately 2 mSv per year (mSv = miliSievert, this unit indicates the burden on the human body; thus the effect on the human body of the amount of radioactivity administered). The additional radiation burden in this study due to the administration of approximately 3.7 MBq radiolabeled EMA401 is calculated to be 0.17 mSv. This is approximately 8.5% of the average annual radiation burden.

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
- 40-55 yrs, inclusive
- BMI: 18.0-30.0 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study. Donation or loss of 50 mL or more of blood within eight weeks prior to initial dosing, or longer if required by local regulation.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2017
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	26-06-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2017
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	EUCTR2016-004705-13-NL
CCMO	NL62120.056.17