Esketamine Oral Thin Film (OTF) administration * a pharmacokinetic pharmacodynamic study in healthy participants

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Objective: Primary objective: To determine pharmacokinetic profiles of an esketamine oral thin film with 50 or 100 mg esketamine; Secondary objective: (1) To determine the pharmacodynamic profile of an esketamine oral thin film containing 50 or 100…

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

Summary

ID

NL-OMON51122

Source
ToetsingOnline

Brief title
ESKOT

Condition

- Other condition

Synonym
neuropathic pain, pain, PK/PD

Health condition

pijnbehandeling

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,LTS Lohmann Therapie-Systeme AG, Duitsland

Intervention

Keyword: esketamine, ketamine, PK/PD study

Outcome measures

Primary outcome

-Plasma concentrations eskatemine and esnorketamine;

-Antinociceptive responses to pressure pain, electrical pain and heat pain.

Secondary outcome

Response to Bowdle and Bond & Lader questionnaires.

Study description

Background summary

The N-methyl-D-aspartate receptor antagonist ketamine is a potent anesthetic, analgesic and antidepressant, increasingly used at subanesthetic doses to treat different forms of pain, as well as depression. Currently the intravenous route is the predominant form of ketamine delivery with inherent need for a successful, sterile venipuncture by skilled healthcare personnel. This prevents the use of ketamine in the out-hospital setting, particularly in case of acute pain treatment (e.g., breakthrough pain). In the current study we will perform a pharmacokinetic-pharmacodynamic study on the efficacy of an esketamine oral thin film (OTF) in 20 healthy volunteers at a dose of 50 and 100 mg using a cross-over design. We will obtain the following end-points: arterial plasma concentrations of S-ketamine and S-norketamine, antinociceptive responses to pressure pain, electrical pain and heat pain, psychomimetic side effects (measured by the Bowdle and Bond & Lader questionnaires). Additionally, the get an indication of the bioavailability of the esketamine OTF, we will infuse a

low dose esketamine via the intravenous route and measure plasma S-ketamine and S-norketamine concentrations at the end of each experimental session. We hypothesize that esketamine in OTF formulation will produce plasma S-ketamine and S-norketamine concentrations that are associated with antinociception.

Study objective

Objective: Primary objective: To determine pharmacokinetic profiles of an esketamine oral thin film with 50 or 100 mg esketamine; Secondary objective: (1) To determine the pharmacodynamic profile of an esketamine oral thin film containing 50 or 100 mg esketamine with endpoints antinociception and psychomimetic side effects; (2) To determine safety and tolerability of the esketamine oral thin film.

Study design

This study has an exploratory, open-label, crossover and randomized design.

Intervention

Administration of S-ketamine mucosal patch (50 mg and 100 mg)

Study burden and risks

In this open label study, we will assess the pharmacokinetic profile of two doses of an esketamine oral thin film in healthy volunteers. We expect few if any adverse effect but will gain valuable data on the plasma concentration effect profile of this novel form of esketamine administration. Such a formulation will be suitable for treatment of acute and chronic (breakthrough) pain. As such we believe this to be a valid study with a positive risk benefit balance.

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

- aged 18-45 years,
- body mass index > 19 and < 30 kg/m2,
- able to understand the written informed consent form,
- able to communicate with the staff,
- able and willing to complete the study procedures,
- signed the informed consent form,
- deemed suitable by the investigators.
- nonsmoking for the last 3 months.

Exclusion criteria

- Presence or history of any medical or psychiatric disease (incl. a history of substance abuse, anxiety, or the presence of a painful syndrome);
- Use of any medication in the three months prior to the study (incl. paracetamol or other pain killers);
- Use of more than 21 alcohol units per week;
- Use of illegal substances, including cannabis, in the 4 weeks prior to the study;
- A positive urinary drug test or a breath alcohol test at screening or on the morning of the experiment;
- Pregnancy, lactating or a positive pregnancy test on the morning of the experiment;
- Participation in another drug trial in the 60 days prior to dosing.

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):	27-01-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Esketamine
Generic name:	S-ketamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-11-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-01-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	12-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	18-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2020-005185-33-NL

Register	ID
CCMO	NL75727.058.20

Study results

Date completed:	27-05-2021
Actual enrolment:	20