A Two Part Phase I Study to Assess Safety, Tolerability, Systemic Exposure and Effect on Analgesia and Anaesthesia of Single and Multiple doses of TDT 077 in Healthy Older Subjects.

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

Summary

ID

NL-OMON31518

Source
ToetsingOnline

Brief title
Single and multiple rising dose study.

Condition

- Peripheral neuropathies

Synonym
Neuropathic pain

Research involving
Human

Sponsors and support

Primary sponsor: Celtic Pharma Development Services Europe Ltd.
Source(s) of monetary or material Support: Celtic Pharma Development Services Europe Ltd.

Intervention

Keyword: Bupivacaine, Neuropathic pain, Safety and tolerability, Single/multiple dose

Outcome measures

Primary outcome

Part 1A:

Primary objective is to evaluate the safety and tolerability of ascending

single doses of TDT 077 in healthy older male and female subjects.

Part 1B:

To validate the sensitivity of the clinical methods for the assessment of

analgesia and anaesthesia.

Part 2:

Primary objective is to evaluate the safety and tolerability of ascending

multiple doses of TDT 077 in healthy older male and female subjects.

Secondary outcome

Part 1A:

Secondary objective is to evaluate the systemic exposure (PK) of ascending

single doses of TDT 077 in healthy older male and female subjects. The third

objective is to evaluate the magnitude and duration of effect (analgesia and

anaesthesia) of ascending single doses of TDT 077 in older male and female

subjects.

Part 1B:

Not applicable

Part 2:

Secondary objective is evaluate the systemic exposure (PK) of ascending multiple doses of TDT 077 in healthy older male and female subjects. Third objective is to evaluate the magnitude and duration of effect (analgesia and anaesthesia) of ascending multiple doses of TDT 077 in healthy older male and female subjects.

Study description

Background summary

TDT 077 is an investigational product, which is being developed to reduce pain as a result of e.g. diabetes, HIV/AIDS and shingles. It is a combination of bupivacaine (a pain reducer) and Transfersomes®. When TDT 077 is applied to the skin, bupivacaine is transported to the target area by Transfersomes®. There, bupivacaine will bind to the nerve cell (a cell is the smallest unit of which the body consist of, a nerve cell is important for passing through pain signals). Bupivacaine reduces the permeability of the cell. By doing this, the conductivity of the cell is being reduced and thus the pain signals, which pass through by this cell.

Emla® cream is marketed for the indication local anaesthesia of the skin and will only be applied in part 1B of this study.
One gram of Emla® cream contains 25 mg of lidocaine and 25 mg of prilocaine (both aneasthetics). It works in the same manner as bupivacaine (as described above).

Study objective

Part 1A:
Primary objective is to evaluate the safety and tolerability of ascending single doses of TDT 077 in healthy older male and female subjects. Secondary objective is to evaluate the systemic exposure (PK) of ascending single doses of TDT 077 in healthy older male and female subjects. The third objective is to evaluate the magnitude and duration of effect (analgesia and anaesthesia) of ascending single doses of TDT 077 in older male and female subjects.

Part 1B:
To validate the sensitivity of the clinical methods for the assessment of analgesia and anaesthesia.

Part 2:
Primary objective is to evaluate the safety and tolerability of ascending multiple doses of TDT 077 in healthy older male and female subjects. Secondary objective is evaluate the systemic exposure (PK) of ascending multiple doses of TDT 077 in healthy older male and female subjects. Third objective is to evaluate the magnitude and duration of effect (analgesia and anaesthesia) of ascending multiple doses of TDT 077 in healthy older male and female subjects.

Study design

Part 1A:
6 groups of 8 healthy males and females will participate in this part of the trial.
For groups 1-5 the trial consist of a medical screening, an admission period of 5 days, a short visit and a follow up.
For group 7 the trial consists of a medical screening, an admission period of 3 days, a short visit and a follow up

Part 1B:
1 group of 8 healthy males and females will participate in this part of the trial. This part of the trial consist of a medical screening and an admission period of 2 days.

Part 2:
5 groups of 8 healthy males and females will participate in this part of the trial. This part of the trial consist of a medical screening, an admission period of 18 days, 10 short visits and a follow up.

Intervention

In Part 1A of this study (KNL40862) the investigational product will be applied once.

In Part 1B of this study (KNL40862) EMLA will be applied once.

In Part 2 of this study (KNL 40863) the investigational product will be applied twice a day on days 1 to 13 and once a day on day 14.

Study burden and risks

The risks for the volunteers participating in this trial are related to the possible side effects of the investigational product and EMLA. Next, the inconvenience for the volunteer depends on the duration of the admission period, venapunctures and inserting the cannula. All volunteers will be closely monitored by experienced physicians and other staff.

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

• Subjects must voluntarily sign a written informed consent agreement;
• Age 55-75 years except cohort 6B. Age 18-40 for cohort 6B;
• Female subjects should be of non-childbearing potential (surgically sterile or more than 1 year post-menopausal) or if of childbearing potential must be using a medically acceptable form of birth control for the duration of the study;
• Male subjects: you are not able to cause a pregnancy or uses a medically acceptable form of birth control for th duration of the study;
• Subjects must be in good health;
• Body Mass Index (BMI) between 18 and 30 (inclusive), with body weight greater than or equal to 60 kg and less than or equal to 100 kg;
• No clinically significant abnormalities at screening

Exclusion criteria

• Subjects with a known hypersensitivity or allergy to bupivacaine, other local anaesthetics or to any of the excipients in TDT 077 (Part 1A and Part 2);
• Subjects with a known hypersensitivity or allergy to lidocaine and/or prilocain, other local anaesthetics or to any of the excipients in EMLA® hydrophilic cream (Part 1B);
• Subject has any skin irritation or disease that might interfere with absorption of study drug or skin irritation assessment, including eczema, psoriasis, melanoma;
• Subjects with active presence or history of alcoholism or drug addiction;
• Subject has a tattoo or other skin deformities that might interfere with skin irritation assessment;
• Subject has had a surgery within the last 3 months prior to dosing;
• Female subjects that are pregnant or lactating;
• Subjects who have used prescription medication within two weeks prior to the first dosing day, except for contraceptives or HRT;
• Subjects who have used over-the-counter medication (including homeopathic medicines and vitamins), within 96 hours prior to the dosing day;
• Subjects who have been treated with other local anaesthetic therapy within 3 weeks prior to dosing;
• Subjects who smoke more than 10 cigarettes per day and who are unable to abstain from smoking when at the study centre;
• Subjects who participated in an investigational drug study within 3 months prior to the dosing day;
• Subjects who have lost or donated >350 ml of blood within 12 weeks prior to the screening session;
• Subjects who test positive for HBsAg, Anti-HCV or HIV;
• Subjects with a relevant food or drug hypersensitivity or allergy;
• Subjects who are considered unsuitable to participate in the study for any reason in the opinion of the principal investigator.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2008
Enrollment:	96
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	EMLA
Generic name:	Lidocaine en prilocaine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	TDT 077
Generic name:	Bupivacaine

Ethics review

Approved WMO

Date:	11-12-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	14-12-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-03-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-03-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-04-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-04-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-04-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-05-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	23-05-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-06-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2007-006781-15-NL
CCMO	NL20901.040.07