An open- label, multi-site trial to describe the safety and tolerability of oral cebranopadol administered for 26 weeks in subjects with cancer- related pain who have completed treatment in the KF6005/07 trial.

Published: 19-03-2014
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Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41264

Source
ToetsingOnline

Brief title
CORAL-XT - Open label extension trail of the CORAL trial

Condition

- Other condition

Synonym
Pain related to cancer

Health condition

Pijn bij kanker

Research involving
Human

Sponsors and support

Primary sponsor: Grunenthal
Source(s) of monetary or material Support: Gruenenthal GmbH

Intervention

Keyword: cancer, extension study, pain

Outcome measures

Primary outcome

The primary endpoint for this trial is the incidence of treatment emergent

adverse events (TEAEs).

Secondary outcome

The secondary safety endpoint for this trial is the intensity of TEAEs.

The secondary efficacy endpoint for this trial is the average pain intensity

(11-point numerical rating scale [NRS]) in the last week during the Treatment

Period and changes from baseline

Study description

Background summary

Cebranopadol is a highly potent mixed NOP/opioid receptor agonist, currently under development for the indication of severe chronic nociceptive pain requiring opioid analgesia.
To fulfill the European Medicines Agency (EMA) requirements for this indication, a Phase III trial is planned in subjects with chronic moderate to severe pain related to cancer (KF6005/07). The main objective of KF6005/07 is to demonstrate the non-inferior efficacy of cebranopadol compared to morphine sulfate PR.
Given that cebranopadol is intended for chronic use, safety and tolerability data will need to be collected in the targeted population during prolonged

exposure to cebranopadol (ICH E1 guideline).
To meet this requirement, KF6005/09 will include subjects who completed their treatment with morphine sulfate PR or cebranopadol in KF6005/07. These subjects will be given the opportunity to participate in KF6005/09 and receive treatment with cebranopadol for up to approximately 26 weeks.
Given the underlying cancer disease, the anticipated poor survival of the targeted population and the resulting high discontinuation rate, the overall duration of the trial will be limited to approximately 28 weeks.

Study objective

The primary objective of this trial is to describe the safety and tolerability of prolonged exposure to cebranopadol in subjects suffering from cancer related pain

Study design

This is a non-randomized, multi-site, open-label, single-arm Phase III trial to describe the safety and tolerability of oral cebranopadol for 26-weeks in subjects with cancer-related pain who have completed treatment in the KF6005/07 trial.
Estimated date of first subject in/last subject out: Q2 2014/ Q3 2016. Subjects are expected to be in the trial for approximately 28 weeks (approximately 199 days).

Intervention

The IMP will be taken orally twice daily throughout the Titration Phase and the Maintenance Phase. The IMP intake must be documented in the e-diary during the treatment period on a daily basis. The different daily doses during the Titration Phase and the Maintenance Phase will be administered using the available dose strengths of cebranopadol (200 µg, 400 µg, 600 µg) and morphine (15 mg, 30 mg, and 45 mg) and the matching placebo tablets or capsules. The starting dose of cebranopadol will be 200 µg per day. The maximum daily dose of cebranopadol is 1000 µg. The minimum daily dose of cebranopadol is 200 µg. The incremental/decremental dose of cebranopadol is 200 µg per day. The aim of the titration is to reach the subject*s individual optimal dose defined as a balance between self-reported analgesia and side effects. The investigator will have access to each subject*s recordings of daily pain ratings and should take these into account in titration decisions. If the tolerability is considered acceptable by both the subject and the investigator, and there appears to be sub-optimal efficacy, i.e., high pain intensity and/or the need to use rescue medication, the investigator should titrate the subject to a higher dose. If the tolerability is considered unacceptable by the subject or the investigator, the investigator should down-titrate the dose. The selected dose at the end of the Titration phase will be used by the subjects during the Maintenance Phase.

To ensure adequate efficacy assessments, changes in dose during the Maintenance Phase will be prohibited.

Study burden and risks

During hospital visits blood will be drawn. The insertion of the needle for the venipuncture will be experienced unpleasant and\or painful by the patient. There might be hemorrhage at the injection site.
in additon there may be some side effects like nausea, vomiting, fatigue, dizziness, and somnolence (drowsiness).
Besides these side effects, other effects, known for classical opioids (narcotics) may occur under treatment with cebranopadol although a causal relationship is not yet evident. Examples of such opioid-typical effects are low blood pressure, slower heartbeat, decrease in breathing rate, constipation, inability to empty the bladder, and drug withdrawal symptoms upon cessation. All opioid drugs including cebranopadol can cause dependency.

Sometimes people have allergic reactions to drugs that, in severe cases, can lead to death. Some signs of an allergic reaction are
* Rash, difficulty breathing, wheezing, sudden drop in blood pressure, swelling around the mouth, throat, or eyes, fast pulse, sweating, itching.

People who have asthma are more likely to have an allergic reaction to the trial medications than people who don*t have asthma.

Contacts

Public
Grunenthal

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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. Informed consent signed indicating that the subject understands the purpose of and procedures required for the trial and is willing to participate in the trial.
2. Subjects must be at least 18 years of age at the Enrollment Visit (Visit 1).
3. Women of childbearing potential must have a negative pregnancy test at Visit 1 and must not be lactating at Visit 1.
4. Subjects must be willing to use medically acceptable and highly effective methods of birth control. For women of childbearing potential a medically acceptable and highly effective method of birth control is defined as any form of contraception with a low failure rate defined as <1% per year. For example:
* Hormonal contraceptives for the duration of the trial and until for at least 4 weeks after Final Visit.
* An intra-uterine device.
Additional barrier contraception must be used by the partner for the duration of the trial. A double-barrier method should be supplemented by the use of spermicidal agents. Women of non-childbearing potential may be included if surgically sterile (i.e., after hysterectomy) or post-menopausal for at least 2 years and
<=55 years old.
For men:
Men have to use barrier contraception (condom) during sexual intercourse for the duration of the trial. The male subject has to take care that the female sexual partner uses at least 1 additional method of contraception with a low failure rate defined as <1% per year (e.g., oral contraceptives) during this time frame.
5. Subjects who have completed treatment in KF6005/07 and are still in need of around-the-clock pain analgesia with strong opioids.

Exclusion criteria

1. The subject has a clinically significant disease or condition other than cancer which in the investigator's opinion may affect efficacy or safety assessments, e.g., significant unstable cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurological, psychiatric (resulting in disorientation, memory impairment or inability to report accurately) or metabolic disorders

or clinically relevant
history of hypersensitivity, allergy or contraindications to opioid medication or any of the excipients of cebranopadol film-coated tablets.
2. Known to or suspected of not being able to comply with the protocol and the use of cebranopadol.
3. Subjects taking forbidden concomitant medications or not being able to follow the rules of use of concomitant treatment
4. History of torsade de pointes and/or presence of risk factors for torsade de pointes (e.g., heart failure, hypokalemia, bradycardia).
5. Concurrent participation in another trial (except participation in KF6005/07) or planning to be enrolled in another clinical trial (i.e., administration of experimental treatment in another clinical trial) during the course of this trial (this does not include observational studies), or previous participation in this trial.
6. Employees of the sponsor, investigator, or trial site or family members of the employees, sponsor, or investigator.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Cebranopadol
Generic name:	Cebranopadol

Ethics review

Approved WMO Date:	19-03-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-08-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-04-2015
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	24-06-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2013-001877-26-NL
CCMO	NL46489.098.14