A randomized, double-blind crossover trial to investigate the effects of oliceridine and morphine on ventilatory drive and pain relief in healthy older subjects - a population pharmacokinetic/pharmacodynamic modeling study

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21214

Source
NTR

Brief title
CP130-1013 study

Health condition

Pain, Opioid-Induced Respiratory Depression (OIRD), Opioid-related side effects, opioid-related adverse events

Sponsors and support

Primary sponsor: LUMC
Source(s) of monetary or material Support: Trevena Inc. (USA)

Intervention

Outcome measures

Primary outcome

- To evaluate the ventilatory and antinociceptive effects of intravenous doses of oliceridine and morphine by population PK/PD modeling in an older population across a range of body weights including subjects meeting the criteria for being overweight;
- To evaluate the ventilatory and antinociceptive effects of intravenous doses of oliceridine and morphine by population PK/PD modeling as a function of body weight;
- To evaluate the clinical utility of oliceridine as compared to intravenous morphine in an older population across a range of body weights

Secondary outcome

- To evaluate the safety and tolerability of oliceridine administered as single intravenous doses in an older population;
- To evaluate the safety and tolerability of oliceridine administered as single intravenous doses as a function of body weight;
- To compare the effects of oliceridine and morphine on other measures of respiratory function, including end-tidal carbon dioxide (PETCO2), oxygen saturation, and respiratory rate.

Study description

Background summary

Opioid analgesics, the cornerstone of contemporary treatment of acute moderate to severe pain, come with numerous adverse effects, of which respiratory depression is potentially life-threatening.
Classical opioid analgesics, such as morphine, are full agonists at the μ-opioid receptor. After receptor activation, these opioids engage two distinct transduction pathways, the G-protein–coupled signaling pathway and the β-arrestin pathway, with separate pharmacologic effects. The G-protein pathway is primarily involved in analgesia, reward, and liking, whereas the β-arrestin pathway is involved in adverse effects such as respiratory depression and gastrointestinal effects, as well as the attenuation of analgesic effects. Recent
focus has been on the development of a new class of opioids, biased ligands, which are μ-receptor agonists that selectively engage the G-protein–coupled signaling pathway with reduced activation of the β-arrestin pathway. Biased ligands may have an advantage over nonbiased, or non-elective μ-opioid receptor agonists as they may be associated with less respiratory depression. The experimental opioid oliceridine (formerly known as TRV130) is a

biased ligand that has been approved by FDA in the United States for treatment of moderate to severe acute pain. In the current study, we will prospectively compare the utility of the biased ligand oliceridine and the classical opioid morphine, now in an older population.

Study objective

It is expected that oliceridine has a better profile concerning dose-related analgesia and dose-related side effects, compared to morphine.

Study design

Screening, Visit 1-4, post-study evaluation

Intervention

All subjects will be tested 4 times on 4 separate occasions at least 1 week apart. On each visit they will receive one of the following doses:
- Oliceridine 0.5 mg IV
- Oliceridine 2.0 mg IV
- Morphine 2 mg IV
- Morphine 8 mg IV

The following tests/procedures will be performed during each visit:
- Rebreathing
- Blood samples
- Cold pressor test
- VAS (nausea, vomiting, sedation, dizziness, lightheadedness, drug likability)

Contacts

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Eligibility criteria

Inclusion criteria

- Absence of any significant medical, neurologic, or psychiatric illness as determined by the investigators.
- Age 55 yr or older;
- Body mass index (BMI) of 19-35 kg/m2.
- Willingness and competence to sign written informed consent.
- Screening cold pressor test hand removal latencies of > 20 and < 120 seconds

Exclusion criteria

1. Clinically significant medical, surgical, psychiatric or substance abuse condition or history of such condition that would confound the interpretation of data in the study;
2. Clinically significant, immune mediated hypersensitivity reaction or intolerance to opioids;
3. Exposure to opioids or anesthesia within 30 days before the first treatment period of the study;
4. Positive urine drug screen or alcohol breathalyzer test at the screening visit or positive urine dipstick for substances of abuse or alcohol breath test at each visit;
5. Participation in a previous oliceridine clinical study;
6. Participation in another interventional clinical study within 30 days before the first treatment period of the study;
7. Body mass index outside <19 or > 35 kg/m2;
8. Taking any prescribed medication which is considered a strong CYP3A4 or CYP2D6 inhibitor or inducer
9. Any clinically significant clinical laboratory abnormality, including total bilirubin > 2 × upper limit of normal [ULN] or elevated hepatic transaminases (aspartate aminotransferase [AST] □ 1.5 × ULN OR alanine aminotransferase [ALT] □ 1.5 × ULN);
10. Clinically significant abnormality on electrocardiogram, including a QT interval corrected for heart rate (QTcF interval) of > 450 milliseconds, at the screening visit;
11. Clinically significant, immune mediated hypersensitivity reaction or intolerance to 5-HT3 inhibitors;
12. Unsuitable screening HCVR test results (e.g., ability to tolerate the mask, breathe in a regular fashion, increase ventilation in response to increases in inhaled CO2), as judged by the investigators;
13. Alcohol intake of more than 4 units/day or more than 28 units/week;
14. The short version of the Mini Mental State Examination with a score less than 9. The latter exclusion criterion was to prevent that subjects with some form of cognitive impairment participated.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-06-2021
Enrollment:	15
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
No plan described yet

Ethics review

Positive opinion

Date:	02-06-2021
Application type:	First submission

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
NTR-new	NL9524
Other	METC Leiden-Den Haag-Delft. (METC-LDD) : P21.025

Study results