A Randomized, Double-Blind, Placebo-Controlled, 2-Way Crossover, Phase 1 Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Danavorexton in Healthy Subjects Undergoing Opioid-Induced Respiratory Depression

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Primary Objective:• To evaluate the safety and tolerability of danavorexton single IV infusion administered in healthy subjects undergoing OIRD.Secondary Objective:• To assess the PK of danavorexton single IV infusion administered in healthy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON52033

Source
ToetsingOnline

Brief title
Takeda - TAK-925-1021 Study

Condition

- Respiratory disorders NEC

Synonym
Opioid-induced respiratory depression;hypoventilation

Research involving
Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: Takeda (Sponsor)

Intervention

Keyword: Danavorexton, healthy subjects, opioid-induced respiratory depression (OIRD), Phase I

Outcome measures

Primary outcome

Safety and tolerability will be assessed by number of subjects with at least 1

treatment-emergent adverse event (TEAE).

Secondary outcome

The following PK parameters of danavorexton will be estimated:

• Observed plasma concentration at the end of infusion (Ceoi).

• Area under the plasma concentration-time curve from time 0 to time of the

last quantifiable concentration (AUClast).

• Area under the plasma concentration-time curve from time 0 to infinity

(AUC*).

Study description

Background summary

Danavorexton is a novel, highly selective orexin type-2 receptor (OX2R) agonist, which is central to the control of arousal and wakefulness. Clinical studies in sleep-deprived healthy subjects and patients with narcolepsy, idiopathic hypersomnia (IH), and obstructive sleep apnea (OSA) have demonstrated that danavorexton administered via IV was well-tolerated and

improved wakefulness in these populations.The purpose of this study is to assess the safety, tolerability, PK, and PD of danavorexton in healthy subjects undergoing OIRD as well as to assess the effect of danavorexton on OIRD. The information obtained from the present study may become beneficial to patients who have OIRD in the future.

Study objective

Primary Objective:
• To evaluate the safety and tolerability of danavorexton single IV infusion administered in healthy subjects undergoing OIRD.

Secondary Objective:
• To assess the PK of danavorexton single IV infusion administered in healthy subjects undergoing OIRD.

Study design

This study is a randomized, double-blind, placebo-controlled, 2-way crossover study to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of an intravenous (IV) infusion of danavorexton (TAK-925) administered in healthy subjects undergoing opioid-induced respiratory depression (OIRD).

Intervention

Subjects will receive sequentially single IV low and high dose danavorexton or placebo on 2 separate occasions.

Study burden and risks

Danavorexton is a novel, highly selective orexin type-2 receptor (OX2R) agonist, which is central to the control of arousal and wakefulness. Clinical studies in sleep-deprived healthy subjects and patients with narcolepsy, idiopathic hypersomnia (IH), and obstructive sleep apnea (OSA) have demonstrated that danavorexton administered via IV was well-tolerated and improved wakefulness in these populations. The purpose of this study is to assess the safety, tolerability, PK, and PD of danavorexton in healthy subjects undergoing OIRD as well as to assess the effect of danavorexton on OIRD. The information obtained from the present study may become beneficial to patients who have OIRD in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. In the opinion of the investigator, the subject is capable of understanding and complying with protocol requirements.
2. The subject reviews, and signs and dates an informed (electronic) consent form, in addition to any required privacy authorization, before the initiation of any study procedure.
3. The subject is male and aged 18 to 55 years, inclusive, at the screening visit.
4. The subject is a current nonsmoker who has not used tobacco- or nicotine-containing products (eg, nicotine patch) for at least 6 months before the administration of the study drug.
5. The subject has regular sleep-wake habits (eg, routinely spends 6.5 to 9 hours in bed nightly) and regularly goes to bed between 9:00 PM and 1:00 AM, as determined by investigator interviews.

6. A male subject must meet the following birth control requirements:
a) For a male subject who is sterile: no restrictions are required for a vasectomized male subject, provided the subject is at least 1-year postbilateral vasectomy procedure before the first dose of the study drug. If a vasectomy procedure was performed less than 1 year before the first dose of the study drug, the male subject must follow the same restrictions as a male that has not had a vasectomy/sterilization (below). Appropriate documentation of surgical procedures should be provided.
b) For a male subject who is nonsterilized: if sexually active with a female partner of childbearing potential, the subject must agree to use an appropriate method of contraception, including a condom with or without spermicidal cream or jelly. These precautions will begin from the administration of the study drug until 5 half-lives plus 90 days after the administration of the study drug.
c) Male subjects must agree to not donate sperm from the time of study drug administration until 5 half lives plus 90 days after the administration of the study drug.
7. The subject has a BMI >=18 and <=32 kg/m2 at the screening visit.
8. The subject must be judged to be in good health based on results of safety laboratory tests (biochemistry, hematology, and urinalysis testing) performed at the screening visit and on medical history, physical examination, vital-sign measurements, and 12-lead ECG performed at screening and baseline assessments.
9. The subject has no history of hypertension or use of antihypertensive medication. BP must be <140 mmHg (systolic) and <90 mmHg (diastolic); subjects will have a heart rate within the range of 50 to 90 beats per minute at the screening visit. BP will be averaged over 3 readings that are done 10 minutes apart.
10. The subject agrees to refrain from taking excluded medications, vitamins, supplements or dietary products listed in Section 7.3 of the protocol during the study.

Exclusion criteria

- The subject has received treatment with another investigational drug within 3 months before screening, or the subject participated in more than 4 investigational drug studies within 1 year before screening.
- The subject received immunotherapy within the past year.
- The subject has facial hair that could interfere with the seal of a facemask (per investigator or site staff judgment), and is unwilling to shave it off before check-in.
- The subject has a positive test result for hepatitis B surface antigen, HCV, HIV antibody/antigen, or syphilis serum reaction test at screening. Note: subjects with positive HBV or HCV serology may be enrolled if quantitative polymerase chain reaction for HBV or HCV viral RNA is negative.
- The subject has a risk of suicide according to endorsement of Item 4 or 5 of the C-SSRS at the screening visit or has made a suicide attempt in the previous

6 months.
- The subject has a positive alcohol or drug screen at screening or check-in, has a history of alcohol consumption exceeding 2 standard drinks per day on average within the 12 months before screening, or has a history of opioid abuse.
- The subject has caffeine consumption of more than 400 mg/day for 2 weeks before screening (1 serving of coffee is approximately equivalent to 100 mg of caffeine).
- The subject has a screening ECG with a QT interval with Fridericia correction method (QTcF) >450 ms.

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):	15-03-2022
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Danavorexton
Generic name:	Danavorexton
Product type:	Medicine
Brand name:	Remifentanil
Generic name:	Piperidinecarboxylate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-01-2022
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	EUCTR2021-003869-35-NL
CCMO	NL78868.056.21