A phase I, open-label study to assess the pharmacokinetic profile, safety and tolerability of OBE001 after a single oral administration in pregnant women with medically indicated pregnancy termination

Published: 13-03-2014
Last updated: 20-04-2024

Primary objectives: -To evaluate the PK profile of OBE001 when administered orally to pregnant women.Secondary objectives: -To evaluate the maternal safety and tolerability of OBE001 when administered orally to pregnant women.-To evaluate the acute...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Interventional

Summary

ID

NL-OMON40897

Source
ToetsingOnline

Brief title
OBE001 Phase I PK study in pregnant women with indicated termination

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
NA (healthy volunteers)

Research involving

Human

Sponsors and support

Primary sponsor: ObsEva SA
Source(s) of monetary or material Support: ObsEva SA

Intervention

Keyword: OBE001, pharmacokinetic, pregnancy

Outcome measures

Primary outcome

The following pharmacokinetic variables will be calculated for each subject

using the actual sampling intervals (relative to medication administration):

- Maximum concentration (Cmax).

- Area under the plasma drug concentration versus time curve to 24h post-dose

time point (AUC 0-24) and to last measured time point (AUC last).

- Area under the plasma drug concentration versus time curve with extrapolation

to infinity (AUC0-*).

- Time to the maximum concentration (tmax).

- Apparent terminal half-life (t1/2).

- Terminal elimination rate (*el)

- Apparent volume of distribution after non-intravenous administration (Vd/F)

- Apparent total clearance of the drug from plasma after oral administration

(Cl/F)

Secondary outcome

- Number and proportion of women experiencing treatment-emergent adverse events

assessed by safety variables (clinically significant changes in laboratory

safety tests, 12-lead ECGs morphology and time intervals, vital signs and other reported adverse events).

- Number and proportion of fetus experiencing treatment-emergent major cardiac rhythm changes i.e. severe tachycardia (heart rate >= 160 bpm lasting for >= 5 min), bradycardia (heart rate <= 80 bpm lasting for >= 5 min) or cardiac arrest.

- Foeto-maternal exposure ratio at the time of delivery, based on time-matched sample collections from mother and fetus (umbilical cord vein).

Study description

Background summary

The contracting uterus is the most frequently recognized antecedent of preterm birth. Stopping contractions has been the focus of therapeutic approaches. Different classes of drugs have been used for tocolytic therapy. But they are not really adequate due to lack of efficacy or adverse reactions. A safe oral drug for preterm labour is an unmet medical need.
The purpose of this study is to assess the pharmacokinetic profile, the safety, and the tolerability of OBE001, a new tocolytic drug of the pyrrolidine class. OBE001 is competitive and reversible, orally active oxytocin receptor antagonist and shows selectivity over vasopressin receptors. In this study, it will be administered orally in pregnant women with medically indicated pregnancy termination.

Study objective

Primary objectives:
-To evaluate the PK profile of OBE001 when administered orally to pregnant women.

Secondary objectives:
-To evaluate the maternal safety and tolerability of OBE001 when administered orally to pregnant women.
-To evaluate the acute safety of OBE001 for the fetus.
-To assess the placental passage from the mother to the fetus after a single

oral dose of OBE001.

Study design

The study is a prospective, non-randomised, open-label, single dose study investigating the pharmacokinetics and the safety of the oxytocin receptor antagonist OBE001 administered orally at dose of 600 mg (3 x 200 mg) in twelve (12) pregnant women with medically indicated pregnancy termination. The study duration will be up to 15 days per subject (from screening to the end-of-study visit) and will be divided into 3 phases:
- a screening period of up to 7 days (Day -7 to Day -1) before dosing (Day -1 being immediately before Day 1).
- a dosing and PK sampling period (Day 1 and Day 2), in which Day 1 will correspond to the dosing day (single oral dose administration in the morning) and Day 2 to the day of pregnancy termination. PK sampling will be done up to the induced delivery. The subjects will be hospitalized in the clinical unit from the morning to the evening of Day 1 for about 12.00 hour post-dose sampling. Subjects might stay overnight (from Day 1 to Day 2) at the clinical unit, according to the investigator*s and subject*s decision. The subjects will be admitted in the clinical unit in the morning of Day 2 for undergoing pregnancy termination procedure. If delivery doesn*t occur on Day 2 but on Day 3 subjects will stay overnight from Day 2 to Day 3.The subjects will be discharged after the delivery according to the center practice.
- a follow-up post-discharge period up to the End-of-Study visit at Day 8.

Intervention

Single oral intake of 600mg OBE001 (3x200mg) the day prior induced delivery.

Study burden and risks

This study drug can have the following side effects: Headaches, Pain in arms or legs, Common cold, Back pain, Dizziness, Tiredness, Nausea, Increased heart rate, Skin rash.

Contacts

Public
ObsEva SA

Chemin des Aulx 12
Plan-Les-Ouates, Geneva 1228
CH
Scientific

ObsEva SA

Chemin des Aulx 12
Plan-Les-Ouates, Geneva 1228
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.The Subject must provide written informed consent prior to initiation of any study related procedures, as shown by a signature on the volunteer consent form.
2.The Subject must be an adult woman aged from 18 and above at screening.
3.The Subject must be a healthy pregnant female volunteer.
4.The Subject must have a medically indicated pregnancy termination for fetal indication (e.g. genetic abnormality and/or congenital malformation).
5.The Subject must have a pregnancy with a gestational age (confirmed by US scan done prior Week 20+0/7) at the time of planned pregnancy termination being between 14+0/7 (inclusive) week and upper limit for legal pregnancy termination in the center country.
6.The Subject must have a singleton pregnancy.
7.The Subject must be non-smoker or must be a light smoker (less than 5 cigarettes per day). No smoking (or smoking substitute e.g. nicotine patch) is permitted from screening and throughout the study.
8.The Subject must be able to communicate well with the investigator and research staff and to comply with the requirements of the study protocol.

Exclusion criteria

1.The Subject has a current pregnancy with a dead fetus.
2.The subject has a current pregnancy with an expected high risk of fetal death in the coming days, including severe fetal cardiac malformation, fetal cystic hygroma or hydrops fetalis.

3.The Subject had a BMI >= 35 kg/m2 prior to current pregnancy.
4.The Subject has a current body weight < 50kg.
5.The Subject has any condition, including findings in the medical history or in the pre-trial assessments, which in the opinion of the investigator constitutes a risk or a contraindication for the participation of the subject in the trial or that could interfere with the trial objectives, conduct or evaluation.
6.The Subject has any clinically significant abnormality in the results of the screening safety laboratory tests, including AST, ALT, GGT, alkaline phosphatase or total bilirubin above twice upper limit of normal. In case of isolated GGT increase, a single re-test is allowed.
7.The Subject has any clinically significant abnormality in the results of the screening physical examination which in the opinion of the Investigator could interfere with the trial objectives, conduct and evaluation.
8.The Subject has any clinically significant abnormality in the results of the screening gynaecological examination which in the opinion of the investigator could interfere with the trial objectives, conduct and evaluation.
9.The Subject has any clinically significant abnormality on the 12-lead ECG recording at screening.
10.The Subject has any clinically significant abnormality on arterial blood pressure (BP) or heart rate (HR) at screening.
11.The Subject has a known positive result from virology tests for hepatitis B surface antigen (HBsAg) (not due to vaccination), hepatitis B core antibody (HBcAb), hepatitis C virus (HCV) or human immunodeficiency virus (HIV) 1 or 2.
12.The Subject has a history or presence of clinically significant hypertension or other significant cardiovascular abnormality.
13.The Subject has a history or presence of significant kidney disease.
14.The Subject has a history of any significant acute infection in the four weeks before dosing.
15.The Subject has a history of serious allergy (i.e. that required hospitalization or systemic treatment), asthma, allergic skin rash or allergy to any of the ingredients of the OBE001 tablet (see list of ingredients in the Investigator*s Brochure).
16.The Subject has been administered with any experimental drug in the 12 weeks before dosing.
17.The Subject has forfeited her freedom by administrative or legal award or was under guardianship.
18.The Subject has known current problems with drug or alcohol abuse (more than 7 units of alcohol per week, one unit = 280 mL of beer (3-4°), 100 mL of wine (10-12°) or 30 mL of spirits (40°).
19.The Subject has lost or donated more than 400 mL of blood in the 12 weeks before dosing.
20.The Subject has used any prescription drugs or over-the-counter drugs (with the exception of paracetamol (up to 4 g per day), multi-vitamins, iron and folic acid) in the week before dosing, without prior approval from the investigator.
21.The Subject has consumed any substances known to be potent inhibitors or inducers of CYP P450s such as grapefruit juice, grapefruit juice-containing products, and herbal remedies or dietary supplements containing St. John*s Wort, in the week before dosing.
22.The Subject has participated in any previous studies involving oxytocin receptor antagonists during current pregnancy.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	OBE001
Generic name:	OBE001

Ethics review

Approved WMO Date:	13-03-2014
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-06-2014
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-09-2014

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-09-2014
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	EUCTR2013□005048-27-NL
CCMO	NL47768.000.14