A double-blind, placebo controlled, randomised, parallel group study with an open-label cross-over part, investigating safety, tolerability, pharmacokinetics, and pharmacodynamics after single ascending oral doses and a single intravenous dose of the vasopressin V2-receptor agonist FE 201836

Published: 18-06-2015
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON43629

Source
ToetsingOnline

Brief title
FE 201836 SAD and cross-over study

Condition

- Other condition

Synonym
night voiding

Health condition

Nocturia

Research involving
Human

Sponsors and support

Primary sponsor: Ferring
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Nocturia, Placebo, V2-receptor agonist FE

Outcome measures

Primary outcome

- To assess the safety and tolerability of single intravenous and oral doses of

FE 201836

- To determine single oral dose pharmacokinetics of FE 201836

- To determine single intravenous dose pharmacokinetics of FE 201836

- To determine single intravenous dose pharmacodynamics of FE 201836

- To study the metabolite pattern of FE 201836 in plasma and urine

- To collect data for analysis of the effect of FE 201836 on the QT interval

- To compare intravenous single dose pharmacokinetics and pharmacodynamics of

FE 201836 with desmopressin

Secondary outcome

n/a

Study description

Background summary

FE 201836 is a new investigational compound that may eventually be used for the treatment of excessive night-time urination. FE 201836 is expected to reduce urinating by decreasing the water excretion in the kidneys. FE 201836 stimulates the vasopressin V2 receptor, which regulates the body*s water retention and constriction of vessels. A drug with a similar mode of action (desmopressin) is currently available for the treatment of excessive night-time urination. However, desmopressin is known to decrease sodium levels in the blood (hyponatremia); in some cases some to a severe extent. FE 201836 is designed to be eliminated from the body more quickly and predictably than desmopressin, thus reducing the risk of hyponatremia.
This is the first time that FE 201836 is being given to humans.

Study objective

The purpose of the study is to investigate to what extent FE 201836 is tolerated. It will also be investigated how quickly and to what extent FE 201836 is absorbed and eliminated from the body (this is called pharmacokinetics). Also the effect on urine production (this is called pharmacodynamics) will be investigated.

This study is divided in 2 parts (Part 1 and Part 2). Part 1 studies the tolerability and pharmacokinetics after single dose administration of FE 201836 in 40 healthy volunteers. Part 2 studies the effect of FE 201836 on urine production after an intravenous (i.v. = via a blood vessel) infusion of FE 201836. Part 2 is performed in 2 groups: one group of 12 healthy male and female volunteers and one additional group of 8 healthy male and female volunteers (referred to with Part 2A). The remainder of this document only refers to Part 2A.

Study design

Part 1:
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center in Zuidlaren for 3 days (2 nights).

Part 2:
The actual study will consist of 3 periods. Each period the volunteer will stay in the clinical research center in Zuidlaren for 3 days (2 nights). There will be a resting period of at least 2 days between each period. In each period, the volunteer will receive the study compound on Day 1 and will leave the clinical research center on Day 2.

Part 2A;
The actual study will consist of 1 period during which you will stay in the clinical research center in Zuidlaren for 3 days (2 nights).

Intervention

Part 1:
during this research the volunteer will receive FE 201836 or placebo as a 20 ml oral solution following a night of fasting.

Part 2:
in period one and 3 the volunteer will receive the study drug as a one hour 20 mL infusion (FE 201836 in period one and demopressine in period 3). 2 hours before the IV infusion the volunteer will undergo a waterloading procedure. In period 2 he will receive FE 201836 as a 20 mL oral solution.

Part 2A:
The study will consists of 1 period during which you will receive a 1 hour i.v. infusion of a dose in the range of 0.2-1.0 µg FE 201836. The dose of FE 201836 will be determined based on the safety and pharmacokinetic results in Part 1 and 2.

Study burden and risks

As FE 201836 will be administered to man for the first time in this study, adverse effects of FE 201836 in man have not been reported to date. However, FE 201836 has been studied in animals (rats and dogs). Up to the highest dose tested in animals, no side effects were noted other than minimal abnormalities at cellular level in kidney tissue and a minimal reduction in body weight gain at the high dose level of FE 201836 tested in rats (500 µg/kg/day for 28 days). In dogs a transient increase in heart rate and contractility was observed at a dose of 50 µg/kg FE 201836.

The most common side effects reported in man for compounds with a similar mode of action are: headache, dizziness, increased blood pressure, nausea, abdominal pain, diarrhea, constipation, vomiting, water retention and tiredness. One rare adverse event is hyponatremia. Hyponatremia may be preceded or accompanied by headache, nausea, vomiting, weight gain, confusion and drowsiness. Therefore, your blood will be monitored closely for hyponatremia during the study.

Risks associated with catheterization are a feeling of urgency (caused by the tube) and urinary tract infections. Rare complications are urethral strictures and sepsis.

Procedures: pain, minor bleeding, bruising, possible infection

Contacts

Public
Ferring

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DK
Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- healthy male or female
- 18-45 years old inclusive
- BMI between 18.5 - 29.9 kg/m2
- non smoker

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90
days before the start of this study or being a blood donor within 60 days from the start of the study. In case of

donating more than 1.5 liters of blood in the 10 months prior the start of this study

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-07-2015
Enrollment:	76
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Desmopressin
Generic name:	Desmopressin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	FE 201836
Generic name:	FE 201836

Ethics review

Approved WMO

Date:	18-06-2015
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-01-2016
Application type:	Amendment
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	EUCTR2015-001366-26-NL
CCMO	NL53612.056.15