An open-label, two-period, fixed sequence study to evaluate the effects of multiple oral doses of AFQ056 on the pharmacokinetics of a monophasic oral contraceptive in healthy female volunteers

Published: 07-10-2010
Last updated: 04-05-2024

* To examine how multiple oral doses of the test compound (an experimental medication) will be taken up by the body, metabolized and excreted by the body in combination with the oral contraception pill which consists of ethinyl-estradiol and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON36456

Source
ToetsingOnline

Brief title
CAFQ056A2133

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Neurological disorders NEC

Synonym
Fragile X Syndrome (FXS), interaction study, mental retardation

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma AG

Intervention

Keyword: Healthy female subjects, Interaction, OC, Open-label

Outcome measures

Primary outcome

To assess the effect of multiple oral doses of test compound (100 mg b.i.d.) on the PK of a single dose of a monophasic oral contraceptive (OC), containing ethinyl estradiol (30µg EES) and levonorgestrel (150µg LVG) in healthy female volunteers.

Secondary outcome

To assess the safety and tolerability of multiple, oral doses of b.i.d. test compound in combination with a single dose of a monophasic OC in healthy female volunteers

Study description

Background summary

The test compound is an experimental (or investigational) drug which has not been registered as a medicine. This drug is being developed by the Sponsor for the treatment of Fragile X Syndrome and for some aspects of Parkinson*s Disease. Fragile X syndrome is a genetic syndrome which results in a spectrum of characteristic physical and intellectual limitations and emotional and behavioral features which range from severe to mild in manifestation like learning difficulties, speech impairments, attention problems and epilepsy. Parkinson*s disease is a degenerative disorder of the central nervous system

that often impairs the sufferer's motor skills, speech but also other functions like in Fragile X Syndrome.

The test compound is a so called *metabotropic glutamate receptor 5 inhibitor* which means that it works on blocking certain signaling proteins in the brain

Study objective

* To examine how multiple oral doses of the test compound (an experimental medication) will be taken up by the body, metabolized and excreted by the body in combination with the oral contraception pill which consists of ethinyl-estradiol and levonorgestrel.
* To investigate the safety and tolerability of multiple oral doses of the test compound (the test medication).

Study design

This trial is a open-label, two-period, fixed sequence study.

Intervention

30 healthy female subjects will participate in this trial. On day 1 and 18 an oral contraceptive tablet will be administered. On day 9, 25mg test compound will be administered twice daily, on day 10, 50mg test compound will be administered twice daily, on day 11, 75mg test compound will be administered twice daily and on on days 12-20 100mg test compound will be administered twice daily.

Study burden and risks

The test compound has been previously tested in humans and was generally well tolerated. The test compound has been administered to humans in eight single dose studies and in seven multiple dose studies (in total about 500 healthy subjects and patients). The dosage was between 5 mg and 800 mg, single- and multiple doses. Safety data and data to adverse events result from these studies. The highest *well tolerated* dosage which has been given to humans over several days is 100 mg twice a day.

The most commonly reported adverse events were brain related and included: headache, dizziness, fatigue, insomnia, feeling drunk, blurred vision, hypoaesthesia, nausea and euphoric mood. In addition, visual hallucinations or illusions were also reported in healthy subjects.
In general, the frequency and importance of adverse events tended to diminish over days in multiple dose studies. Studies on subjects and patients with multiple doses of 150 mg test compound twice a day have shown a higher number of adverse events that were central nervous system related. In general no

clinically-relevant, drug-related changes in any ECG parameters, vital signs (heart rate, blood pressure, body temperature, pulse rate) and laboratory findings were observed.

The dose level is selected on the basis of research results in animals and humans. The risk to health at these dose levels is limited but you may experience one of the above mentioned side-effects or other symptoms not previously reported. Your health will be closely monitored during the trial to minimize these risks.

A death of a 77 year old patient with Parkinson's disease during participation in another study with the test compound was reported. This patient had received the test compound twice-daily for 18 days. Prior to the first intake of the test compound the patient had shown an abnormal ECG finding. As there was no autopsy undertaken, the reason for this death remains unclear. To maximize your safety throughout the study, thorough cardiovascular monitoring will be carried out during the study. A transient ischemic attack and paraesthesias has been recently reported for a 50 year-old female patient with Parkinson's disease during participation in another study with the test compound . The patient was reported to have completely recovered.

Contacts

Public
Novartis

Forum 1, Novartis Campus
CH-4056 BAsel
CH
Scientific
Novartis

Forum 1, Novartis Campus
CH-4056 BAsel
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy female subjects, 18 to 40 years of age, BMI 18 - 30 kg/m2, OC containing EES (30µg)/LVG (150µg) for a least of three cycles prior to screening.

Exclusion criteria

Subjects that are pregnant, post-menopausal, breast-feeding or have stopped- breastfeeding less than 6 months before screening, smoker, clinically significant abnormalities during screening and baseline

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-10-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Microgynon
Generic name:	Oral contraceptive EES (30) and LVG (150)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-10-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-02-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-02-2011
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	EUCTR2010-021937-29-NL
CCMO	NL33982.056.10