An open-label, multiple dose, randomized, two-way crossover study to evaluate the effects of BGG492 on the pharmacokinetics and pharmacodynamics of a monophasic oral contraceptive in healthy female volunteers

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON34415

Source
ToetsingOnline

Brief title
CBGG492A2115

Condition

- Other condition

Synonym
Epilepsia, falling disease

Health condition

Epilepsie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: females, interaction, OC

Outcome measures

Primary outcome

Pharmacokinetics of EES and LVG on dag 14

Secondary outcome

Pharmacokinetics of EES and LVG on dag 21

PK profile of BGG492

Pharmacodynamics

Safety

Study description

Background summary

BGG492 is not registered as a medicine and is a drug that is being developed for the treatment of epilepsy. Epilepsy is one of the most common neurological disorders, with a life time prevalence in excess of 1% of the world population. Despite the fact that there are several anti-epileptic drugs on the market, there is still a high medical need for improved treatments of epilepsy since about 30-40% of patients is inadequately controlled or suffer from drug side effects. The development of anti-epileptic drugs with new mechanisms of action is therefore desirable.

BGG492 is a so called orally active AMPA receptor antagonist of which means that it works on blocking certain signaling proteins in the brain. BGG492 is showing anticonvulsant activity in several animal models of epilepsy and first positive results in the interim analysis of an ongoing a single dose proof of concept trial in patients with light sensitive epilepsy.

Study objective

The purpose of this investigation is:
• To examine how the new drug BGG492 (study medication) will be absorbed, metabolized and excreted by the body in combination with the contraception pill which consists of ethinyl-estradiol and levonorgestrel.
• To assess the effect of BGG492 given on the effect of an oral contraceptive determined by the hormones FSH, LH, estradiol and progesterone concentrations and transvaginal ultrasound.
• To assess the safety and tolerability of BGG492 given three times daily in co-administration with once daily dosing oral contraceptive
• To assess the cardiac safety after repeated administration of BGG492 given three times a day

Study design

This trial is an open label, randomized, two way cross-over study

Intervention

24 healthy female test subjects will participate in this trial. Depends on the allocation to the treatment group these 24 women will receive either 1 tablet of OC given concomitanly with 3 hard gelatine capsules of BGG492 given three times a day in dose of 100 mg for a period of 21 days in period 1 or period 2. Alternatively they will receive only OC tablet

Study burden and risks

So far, four clinical studies with BGG492 were conducted in a total of 247 healthy subjects. The results of these clinical studies regarding safety and therein observed unwanted events (side effects) as dizziness, fatigue, sleepiness and balance disorder. In some subjects, changes in their ECG (electrocardiogram) occurred at different time points after the administration of BGG492. These were for example a slower heart beat or additional heart beats of mild intensity that were recorded by the ECG, but induced no symptoms.

All these described unwanted effects in previous clinical studies were temporary and disappeared without any treatment. No clinically significant deviations of vital signs (blood pressure, pulse), ECG (measurement of the

electrical heart activity) or the physical and neurological examination were reported.

In another clinical study, an interaction between BGG492 and the marketed drug cyclosporine was investigated in 30 healthy subjects. Reported were the already known neurological unwanted effects of BGG492. No increase of unwanted effects with a combined administration of cyclosporine was reported.

Currently, three (3) patient studies are conducted in the indications epilepsy and migraine. In general, BGG492 was tolerated well. However, in a currently ongoing proof-of-concept study [CBGG492A2204] investigating a single dose of 250 mg BGG492 in patients with acute migraine, one female patient developed nystagmus along with dizziness and unsteady gait 4 hours after intake of study medication. All events resolved 3 hours after onset. Nystagmus had been observed for the first time and in this case it was classified as serious since the patient was hospitalized overnight for observation, i.e. the event was classified as a suspected unexpected serious adverse event (SUSAR).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Young females, 18-40 years, BMI 18-29 kg/m2, non-smokers, OC-user

Exclusion criteria

Clinical 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):	16-08-2010
Enrollment:	24
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:	03-08-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-08-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-08-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-02-2011
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	EUCTR 2010-019967-1-NL
CCMO	NL32794.056.10