A multicenter, randomized, double-blind, placebo-controlled, cross-over, proof of concept study comparing the effects of both single dose and repeated dosing treatment for 2 weeks of test compound in patients with chronic subjective tinnitus

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To examine the multiple dose effects of the study medication test compound in tinnitus after a 2-week treatment.

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

Summary

ID

NL-OMON36809

Source
ToetsingOnline

Brief title
CBGG492A2210

Condition

- Other condition
- Neurological disorders NEC

Synonym
n.a., Tinnitus

Health condition

Epilepsy, Tinnitus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cross-over, double-blind, placebo-controlled, proof of concept

Outcome measures

Primary outcome

To examine the multiple dose effects of the study medication test compound in

tinnitus after a 2-week treatment.

Secondary outcome

N.A.

Study description

Background summary

The test compound is an experimental (or investigational) drug which has not been registered as a medicine for the treatment of people with epilepsy, migraine and tinnitis.

Study objective

To examine the multiple dose effects of the study medication test compound in tinnitus after a 2-week treatment.

Study design

A multicenter, randomized, double-blind, placebo-controlled, cross-over, proof of concept study comparing the effects of both single dose and repeated dosing treatment for 2 weeks of test compound in patients with chronic subjective tinnitus

Intervention

The patient will take 1 capsule with 50 mg test compound each, 3 times a day for 6 weeks. The patient will not be informed when exactly the first treatment period will end and the second treatment period will start. However, the patient will receive the test compound only for a maximum duration of 15 days.

Study burden and risks

Risks emerge from potential side effects of the study medicine and from taking blood during the patient*s visits at the clinic. To date, the test compound was investigated in healthy subjects as well as in patients with epilepsy and migraine. The highest single dose tested was 450 mg and the highest multiple dose was 150 mg three times a day administered for 14 days. The most frequently observed side effects, deemed to be related to the test compound, were dizziness, fatigue, sleepiness, headaches and balance disorder. The majority of these adverse events were observed in subjects receiving single doses of 250 mg and higher or receiving a multiple dose treatment of 150 mg three times a day. In some healthy subjects, changes in their ECG occurred at different time points after the administration of the test compound. These were (for example) a slower heart beat or additional heart beats of mild intensity recorded on the ECG, but no induced symptoms were noted. Since in some subjects such ECG changes were seen already before intake of the test compound, it is currently not fully clear whether the ECG changes were caused by the test compound.

In a few healthy subjects transient dizziness during standing was observed. Most probably this was caused by a short-lasting decrease of blood pressure.

In a study investigating a single dose of 250 mg test compound in patients with acute migraine (clinical part completed recently), two female patients experienced dizziness and unsteady gait. One of these patients additionally developed nystagmus (i.e. involuntary eye movement) about 4 hours after intake of study medication. Both patients were hospitalized overnight as a precaution. All events resolved 3 hours after onset.

In a recently completed study, one healthy subject receiving a dose of 150 mg three times a day test compound for 14 days showed a modest (about two-fold the upper limit of normal [ULN]) increase of liver enzymes. The increase started on day 6 of treatment, remained at approximately 2-fold ULN for the rest of the treatment period and decreased to normal again within a few days after completing the treatment.

All these described unwanted effects seen in previous clinical studies were transient and disappeared without any treatment. Except for the few cases of dizziness most probably caused by a short-lasting decrease of blood pressure and the single case of increase in liver enzymes, there were no relevant deviations of vital signs (blood pressure, pulse), ECGs (measurement of the electrical heart activity), laboratory parameters or in the physical and neurological examination.

A substance similar to the test compound caused transient vision problems, mainly hypersensitivity to light, in earlier clinical studies. So far, this was not observed after the intake of the test compound.

The dose to be administered in the present study (100 mg BGG492 three times a day) was selected on the basis of results derived from studies in healthy subjects and epilepsy patients. Due to several subjects enrolled in this study experiencing adverse events like dizziness, tiredness, disturbed coordination (gait disturbance), nausea and vomiting (some of them deteriorating the performance of daily activities) and which may be related to the study medication intake, Novartis has decided to reduce the dose to 50 mg three times a day (or 1 capsule three times a day), from the start of the study for subjects enrolled in the study after 27 June 2011. The risk to health at this dose level is limited but the patient may experience one of the above mentioned side-effects or other symptoms not previously reported. The patients health will be closely monitored during the trial to minimize any risks.

Problems or side effects not now known to date could also occur. The patient*s will be given any new information that may affect the patient*s willingness to start or continue in the study.

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

Male and female patients, age 18 to 75 years (included), diagnosed with THI severity grade 3, 4 or 5 (moderate, severe or catastrophic), chronic (> 6 months and < 36 months) subjective tinnitus at Screening

Exclusion criteria

Patients with diagnosed anxiety disorders, depression, schizophrenia or other significant psychiatric diseases requiring current drug treatment or patients who required treatment in the previous 3 months for these diseases. Patients diagnosed THI severity grade equal to 2 or 1 at screening

Study design

Design

Study phase:	2
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):	27-01-2011
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	19-11-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-11-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-08-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-08-2011
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	EUCTR2010-022166-27-NL
CCMO	NL34542.056.10