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Pragmatic trial to find out if the additional use of Ginkgo Biloba extract EGb 761® in patients with chronic tinnitus may influence the properties of the tinnitus retraining therapy positively.

Submission date 23/05/2014	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 06/06/2014	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 09/06/2017	**Condition category** Ear, Nose and Throat	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and aims:
Tinnitus is what happens when a person has the perception of sound within the ear (ringing of the ears) when no actual sound is present. It is not a disease but a condition that may have one of a number of different causes. It can be managed using tinnitus retraining therapy (TRT), which uses a patients natural ability to get used to a sound so it becomes part of their subconscious (rather like getting used to the hum of an air conditioning unit in an office, for example), enabling them to cope with the condition. This aim of this trial is to find out whether the herbal Ginkgo Biloba extract EGb 761® has a positive (enhancing) effect on the success of TRT training. Both TRT and EGb 761® are long-term available treatments for tinnitus that may be taken separately or together. This trial is designed to compare how successful the combination of TRT and EGb 761® at is at treating the condition compared with the TRT treatment alone.

Who can participate:
Male and female participants, suffering from chronic tinnitus (that is, for more than 3 months) and aged at least 30 years.

What does the trial involve?
Participants are randomly allocated into one of two groups. Group 1 undergo TRT treatment together with EGb 761® for 6 months. Group 2 undertake just the TRT treatment. All participants then visit an outpatient clinic at the start of the trial and then after 6, 12 and finally 24 weeks at which they are asked to fill in some self-rating questionnaires (for details see "Interventions" section). At the end of the treatment period all participants are asked to take part in another 6 months follow-up period with 2 additional visits after 36 and 48 weeks. During this period they continue the TRT exercises they have learned during treatment period on their own and without any further medication. They then fill in questionnaires that ask about their mental well-being and tinnitus.

What are the possible benefits and risks of participating:
All participants will benefit from the intensive and detailed diagnostic measures at their first visit. All participants may also benefit though a reduction in tinnitus symptoms and an improvement in their general and mental well-being. No side effects during or after TRT treatment are known. EGb 761® may cause gastrointestinal symptoms, headache and allergic skin reactions, but these are usually mild in nature. Bleeding has been observed in individual cases with Ginkgo preparations, some of unknown origin and quality and in some instances when taken with anti-platelet or anti-coagulant drugs. However, specific clinical trials with EGb 761® at dose levels up to 480 mg per day have shown no effect on coagulation parameters or platelet function. There is hardly any risk associated with the tests and examinations required by this trial protocol, except for a small risk of infection during blood sample drawing.

Where is the trial run from:
The trial will be performed in 5-10 ENT specialists´ practices in the German speaking part of Switzerland.

When is the trial starting and how long is it expected to run for:
From June 2014 to June 2016

Who is funding the trial?
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Who is the main contact:
Susanne Kraft (Project Director)
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
523079.01.101

Study information

Scientific Title
Pragmatic trial to assess the possibility of enhancing the effectiveness of tinnitus retraining therapy (TRT) by concomitant treatment with Ginkgo Biloba extract EGb 761® in patients with chronic tinnitus

Study objectives
As no prior information from randomised clinical trials exists about the possibility of enhancing the effectiveness of tinnitus retraining therapy by concomitant treatment with Ginkgo Biloba extract EGb 761®, no formal hypotheses are formulated and the data will be presented descriptively. Therefore, the association of Ginkgo Biloba extract EGb 761® with measures assessing the effect of the enhancement will be analysed in an explorative manner.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Kanton Zurich, 05 May 2014, ref. KEK-ZH-Nr. 2013-0550

Study design
Randomised, pragmatic, open-label, controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
The patient information sheet is available at Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Health condition(s) or problem(s) studied
Chronic Tinnitus

Interventions
The trial will involve 300 outpatients (male and female) at 5-10 trial sites (ENT specialists) in Switzerland. Trial duration per patient is 6 months up to 12 months, if the participant agrees to a 6 months follow-up period.

The participants are randomly devided into two treatment groups:
Group 1: receiving tinnitus retraining therapy (TRT) with additional intake of the investigational product EGb 761® (240 mg/day)
Group 2: Tinnitus retraining therapy (TRT) only

All participants undergo the following trial visits:
1. Screening (day -7)
2. Baseline (day 0): randomisation
3. Week 6
4. Week 12
5. Week 24 (close-out-visit for randomized treatment period, start of follow-up period)
6. Week 36
7. Week 48 (end of follow-up).

Interventions:
Efficacy:
1. Otological examinations (tone and speech audiometry, maskability)
2.Tinnitus Questionnaire (TQ)
3. Hospital Anxiety and Depression Scale (HADS)
4. Perceived Stress Questionnaire (PSQ)
5. Sheehan Disability Scale (SDS)
6. Hyperacusis Questionnaire (GÜF)
7. 11-Point Box Scales for tinnitus loudness and annoyance

Safety (Screening and Week 12):
1. Physical examinations / Vital Signs
2. Safety laboratory examinations

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Due to the trial hypothesis no differentiation between primary and secondary outcome variables is made.
Outcome variables:
1. Pure tone and speech audiometry
2. Tinnitus Questionnaire (TQ)
3. Hospital Anxiety and Depression Scale (HADS)
4. Perceived Stress Questionnaire (PSQ)
5. Sheehan Disability Scale (SDS)
6. Hyperacusis Questionnaire (GÜF)
7. 11-Point Box Scales for tinnitus loudness and annoyance

Secondary outcome measures
See above

Overall study start date
30/06/2014

Completion date
30/06/2016

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Outpatients aged ≥ 30 with unilateral or bilateral, chronic tinnitus (duration more than 3 months)
2. Tinnitus in the context of hearing loss, noise or mental stress
3. Tinnitus is the main complaint; other cochlear or vestibular symptoms may be present but less annoying
4. Tinnitus stage according to Biesinger 2 or higher at baseline
5. Written informed consent to participate in the clinical trial, to randomised treatment allocation and to data recording in accordance with applicable laws. Participants must be of age and they shall be able to realize the character, importance and consequences of the clinical trial and to align their volition with it.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
300 outpatients

Key exclusion criteria
1. Participation in another experimental drug trial at the same time or within the past 4 weeks before enrolment
2. Any treatments for tinnitus taken currently or within 4 weeks before randomisation
3. Acute or chronic otitis media or vestibular neuritis
4. Drug-induced tinnitus
5. Ongoing psychiatric disorder, such as major depression, generalized anxiety disorder, schizophrenia, etc
Of note: Symptoms of depression or anxiety or other behavioural or psychological symptoms at sub-syndromal level and not requiring treatment with psychotropic drugs are permitted.
6. Severe cardiac or circulatory disorder
- severe (Canadian Cardiovascular Society stage IV) or unstable angina pectoris
- decompensated congestive heart failure (NYHA stage IV)
- uncontrolled hypertension with systolic blood pressure above 180 mmHg and/or diastolic blood pressure above 115 mmHg
- clinically significant cardiac arrhythmias (Lown classes IVb and V, bifascicular bundle branch block).
7. Severe renal or hepatic dysfunction (serum creatinine or serum ASAT, ALAT or gamma-GT

above 3 times the upper limit of the reference range) or coagulation disorder
8. Insulin-dependent diabetes mellitus
9. Intake of drugs not permitted during participation in the study, in particular, insulin, psychoactive drugs, perfusion-enhancing drugs, cognition enhancing drugs or anti-cholinergic drugs (for details see section 6)
10. Active malignant disease (exception: prostate cancer which does not require other than hormone treatment within the next 6 months)
11. Known hypersensitivity to Ginkgo biloba extract or to excipients contained in the tablets
12. Active peptic ulcer disease or any gastrointestinal disease with potential impairment of the absorption of orally applied drugs (e.g. Billroth I/II, Crohn's disease, ulcerative colitis, any kind of enterectomy)
13. Female patients, who are pregnant, breast-feeding or of childbearing potential without safe contraception (hormonal contraception, oral or transdermal, and intra-uterine devices are considered sufficiently safe; child-bearing potential can be denied in case of postmenopausal state for at least 2 years, hysterectomy, bilateral tubal ligation or bilateral oophorectomy).

Date of first enrolment
30/06/2014

Date of final enrolment
30/06/2016

Locations

Countries of recruitment
Switzerland

Study participating centre
Facharzt für Hals-Nasen-Ohrenheilkunde
Landquart
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7302

Sponsor information

Organisation
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Sponsor details
Willmar-Schwabe-Str. 4
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Sponsor type

Industry

Website
http://www.schwabepharma.com

ROR
https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration