

# 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.

<b>Submission date</b> 23/05/2014	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 06/06/2014	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 09/06/2017	<b>Condition category</b> Ear, Nose and Throat	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 patient's 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® 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 through 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)

susanne.kraft@schwabe.de

## Contact information

### Type(s)

Scientific

### Contact name

Dr Andreas Schapowal

### Contact details

Facharzt für Hals-Nasen-Ohrenheilkunde  
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Landquart  
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7302

## Additional identifiers

### Protocol serial number

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

## Study type(s)

Treatment

## 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 divided 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(s)

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

## Key secondary outcome(s)

See above

## Completion date

30/06/2016

## Reason abandoned (if study stopped)

Participant recruitment issue

# Eligibility

## Key inclusion criteria

1. Outpatients aged  $\geq 30$  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

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Sex**

All

### **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

Switzerland

7302

## Sponsor information

**Organisation**

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

**ROR**

<https://ror.org/043rrkc78>

## Funder(s)

**Funder type**

Industry

**Funder Name**

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

## Results and Publications

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration