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Clinical trial to explore treatment effects of Ginkgo biloba extract EGb 761® in patients with chronic tinnitus and effect modification by etiology, biological factors and concomitant pathologies

Submission date
05/10/2016

Recruitment status
No longer recruiting

Registration date
14/10/2016

Overall study status
Completed

Last Edited
12/01/2026

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Tinnitus is where a person experiences a ringing or buzzing sound in one or both ears. It is not regarded as an illness in itself but as a symptom of different diseases. In most cases tinnitus is associated with damage to the hearing system, although it can also be associated with other factors, such as some head injuries, exposure to certain drugs, nerve damage or blood-flow problems. EGb 761® is a dry extract of Ginkgo biloba (maidenhair tree) which may be used for tinnitus treatment. All the clinical findings up to date suggest that EGb 761® may not only be effective for tinnitus symptoms, but also help improve feelings of low mood or anxiety associated with tinnitus. Depending on the cause, influence of risk factors, symptom characteristics and chronicity (length of the symptoms), EGb 761® may be more or less effective. The aim of this study is therefore to explore what influences the effectiveness of treatment with EGb 761®.

Who can participate?
Adults with long term (chronic) tinnitus.

What does the trial involve?
After a screening period of 7 consecutive days where medical history and tinnitus symptoms are recorded, all participants receive tablets containing EGb 761® to take twice a day for 24 weeks. Throughout the study and side effects from the medication are monitored by the patient and care team. After 12 and 24 weeks, participants complete a number of questionnaires in order to find out if the medication has helped reduce their symptoms.

What are the possible benefits and risks of participating?
All participants will receive EGb 761® treatment, which is expected to help reduce or cure their tinnitus symptoms. Therefore, participants may benefit from an improvement in their quality of

life. They may also benefit from a detailed and wide tinnitus diagnostic. Blood tests may cause mild pain and can provoke bruises or tenderness in the extraction area. As EGb 761® is well tolerated according to the data gathered so far, there is no major risk to taking EGb 761®. There is also a small risk of upset stomach, headache and allergic skin reactions (usually mild). There is also a risk that bleeding disorders may also occur during treatment with EGb 761®.

Where is the study run from?
Centrum Medyczne LIMED (lead centre) and 11 other medical centres in Poland (Poland)

When is the study starting and how long is it expected to run for?
December 2015 to May 2018.

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

Who is the main contact?
1. Mrs Annette Wassmer (public)
2. Dr Robert Hoerr (scientific)

Contact information

Type(s)
Public

Contact name
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Type(s)
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Additional identifiers

Clinical Trials Information System (CTIS)
2016-000315-32

Protocol serial number
523079.01.113

Study information

Scientific Title
Clinical trial to explore treatment effects of Ginkgo biloba extract EGb 761® in patients with chronic tinnitus and effect modification by etiology, biological factors and concomitant pathologies

Study objectives
The aim of this study is to explore whether causes, risk factors, chronicity, characteristics of tinnitus and accompanying features influence the treatment effect of EGb 761® in terms of improvement and response rates and to identify groups of patients that benefit most of EGb 761® treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee at Silesian Medical Chamber in Katowice, 15/06/2016, ref: 23/2016

Study design
Multi-centre uncontrolled open-label explorative phase IIb clinical trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
The trial involves 175 participants (male and female). The trial duration per participant is maximum of 26 weeks. Every patient receives 120 mg EGb 761® film coated tablets twice daily during the 24 treatment weeks. All patients undergo the following scheduled visits:
Screening visit: day -7 to day 0, medical history, tinnitus diagnostic (ears-nose-throat examinations, pure tone audiometry, determination of tinnitus loudness and frequency, tinnitus masking, noise discomfort level, safety laboratory tests, electrocardiogram (ECG), vital signs, physical examination
Baseline visit: Day 0, start treatment with EGb 761®, patient questionnaires (TQ, THI, HADS, PSQ, SDS, tinnitus loudness and annoyance), concomitant medications, adverse events
Week 6 Call: Week 6 ± 1, concomitant medications, adverse events

Week 12 Visit: Week 12 ± 1, patient questionnaires, concomitant medications, adverse events
Week 18 Call: Week 18 ±1, concomitant medications, adverse events
Week 24 Visit: Week 24 ± 1, tinnitus diagnostic (ears-nose-throat examinations, audiometry), patient questionnaires, concomitant medications, adverse events, safety laboratory tests, electrocardiogram (ECG), vital signs, physical examination

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Film-coated tablets containing 120mg EGb 761® (Ginkgo biloba extract)

Primary outcome(s)
1. Effectiveness is measured using the Tinnitus Questionnaire (TQ) at baseline, 12 and 24 weeks
2. Effectiveness is measured using the Tinnitus Handicap Inventory (THI) at baseline, 12 and 24 weeks
3. Effectiveness is measured using the 11-point box scales for tinnitus loudness and annoyance at baseline, 12 and 24 weeks
4. Effectiveness is measured using the Pure tone audiometry at screening at 24 weeks
5. Effectiveness is measured using the Determination of tinnitus loudness at screening at 24 weeks
6. Anxiety and Depression are measured using the Hospital Anxiety and Depression Scale (HADS) at baseline, 12 and 24 weeks
7. Stress is measured using the Perceived Stress Questionnaire (PSQ) at baseline, 12 and 24 weeks
8. Effectiveness is measured using the Sheehan Disability Scale (SDS) at baseline, 12 and 24 weeks

Key secondary outcome(s))
1. Serious (SAEs) and non-serious adverse events (AEs) are spontaneously reported by the patient or observed by the investigator continuously throughout the whole trial
2. Vital signs (blood pressure, pulse rate) will be measured in sitting position at baseline, 12 and 24 weeks
3. Safety laboratory results (hematology, coagulation, clinical chemistry and urinalysis) are measured via blood and urine samples at screening and 24 weeks

Completion date
19/12/2017

Eligibility

Key inclusion criteria
1. Outpatient male or female patient at least 18 years old
2. Chronic tinnitus
2.1. May be unilateral or bilateral, with or without concomitant hearing loss
2.2. Grade according to Biesinger is 2 or 3*

2.3. Duration of at least 3 months
3. Written informed consent to participate in the clinical trial, to trial-related treatment and to data recording in accordance with applicable laws

*Grade 2: The tinnitus is mainly perceived in silence and is disturbing under stress and strain.
Grade 3: The tinnitus causes permanent impairment in personal and occupational spheres. Emotional, cognitive and somatic disorders are present.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
187

Key exclusion criteria
1. Participation in another experimental drug trial at the same time or within the past 4 weeks before the baseline visit
2. Tinnitus due to Ménière's disease, vestibular schwannoma or otosclerosis
3. Any other drug treatments for tinnitus taken currently or within 2 weeks before the baseline visit
4. Gingko biloba preparation for any reason taken currently or within 4 weeks before the baseline visit
5. Cognitive behavioral therapy or tinnitus retraining therapy started within 6 months prior to the baseline visit or planned to be started during the course of the trial
6. Acute or chronic otitis media or acute vestibular neuritis
7. Ongoing psychiatric disorder, such as major depression, generalized anxiety disorder, schizophrenia, etc.
Of note: Symptoms of depression or anxiety or other behavioral or psychological symptoms at sub-syndromal level and not requiring treatment with psychotropic drugs are permitted.
8. Ongoing severe cardiac or circulatory disorder:
8.1. Severe (Canadian Cardiovascular Society stage IV) or unstable angina pectoris
8.2. Decompensated congestive heart failure (NYHA stage IV)
8.3. Uncontrolled hypertension with systolic blood pressure above 180 mmHg and / or diastolic blood pressure above 115 mmHg
8.4. Clinically significant cardiac arrhythmias (Lown classes IVb and V, bifascicular bundle branch block)

9. Severe renal or hepatic dysfunction (defined by serum creatinine or serum ASAT, ALAT or gamma-GT above 3 times the upper limit of the reference range in the anamnesis)
10. Ongoing uncontrolled endocrine or hematological disorder
11. Intake of drugs not permitted during participation in the trial, in particular, psychoactive drugs, systemic acting perfusion-enhancing drugs, cognition enhancing drugs, systemic acting anti-cholinergic drugs, regular use of anticoagulants (platelet aggregation inhibitors permitted) during the 2 weeks prior to the baseline visit
12. Ongoing hemorrhagic diathesis or coagulation disorder
13. Seizure within 2 years prior to Baseline Visit or regular use of anticonvulsive drugs
14. Active malignant disease (exception: prostate cancer which does not require other than hormone treatment within the next 6 months).
15. Known hypersensitivity to Ginkgo biloba extract or to excipients contained in the tablets
16. 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)
17. Female patients of childbearing potential without safe contraception (any form of hormonal contraception, intrauterine devices, sexual abstinence and partner sterilization are considered sufficiently safe when used consistently and correctly; child-bearing potential can be denied in case of postmenopausal state for at least 2 years, hysterectomy, bilateral tubal ligation or bilateral oophorectomy)
18. Planned surgical intervention requiring hospitalization during the clinical trial
19. Previous inclusion in the present clinical trial
20. Incapability of understanding nature, meaning and consequences of the clinical trial
21. Patient unable to read and / or write
22. Patients in custody by juridical or official order
23. Patients who are members of the staff of the trial center, staff of the sponsor or involved Clinical Research Organizations (CROs), the investigator him- / herself or close relatives of the investigator

Date of first enrolment
28/10/2016

Date of final enrolment
10/04/2017

Locations

Countries of recruitment
Poland

Study participating centre
Centrum Medyczne LIMED
Tylna 12
Tarnowskie Góry
Poland
42-600

Study participating centre
Grażyna Pulka Specjalistyczny Ośrodek "ALL-MED"
Św. Marka 31/1
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Poland
31-024

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Medical Center Larmed
ul. Lwowska 17 lok. 1 and 2
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Poland
30-548

Study participating centre
Nutricare Sp. z o.o
Rydlówka 42 A/48
Kraków
Poland
30-363

Study participating centre
Promed P.Łach R.Głowacki Spółka Jawna
ul. Entertainment 24a
Kraków
Poland
31-411

Study participating centre
Centrum Medyczne Biotamed Morawska Barbara
ul. Vincent Fields 4a
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32-020

Study participating centre
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Sponsor information

Organisation
Dr. Willmar Schwabe GmbH & Co. KG

ROR
https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr. Willmar Schwabe GmbH & Co. KG

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		23/12/2025	12/01/2026	Yes	No
Basic results			17/06/2020	No	No