ISRCTN02262139 https://doi.org/10.1186/ISRCTN02262139

To compare the efficacy and safety of Ginkgo biloba extract EGb 761® and betahistine in the treatment of vertigo

Submission date
02/02/2012

Recruitment status
No longer recruiting

Registration date
19/03/2012

Overall study status
Completed

Last Edited
04/09/2014

Condition category
Ear, Nose and Throat

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

Plain English summary of protocol

Background and study aims
Vertigo is a type of dizziness, where there is a feeling of motion when one is stationary. The symptoms are due to a dysfunction of the vestibular system in the inner ear. It is commonly associated with vomiting or nausea, unsteadiness, and excessive sweating. Blurred vision, difficulty in speaking, a lowered level of consciousness, and hearing loss may also occur. Symptoms of vertigo can be acute and last then for just a few minutes or hours or it can be chronic, which is a continuous sensation. The beneficial effects of the Ginkgo biloba special extract EGb 761® on vestibular compensation have been demonstrated in preclinical and clinical studies. Patients show significantly better improvement with EGb 761® than with a placebo (dummy) drug. According to early studies, EGb 761® seems to be as effective as betahistine, one of the most popular drugs for treating vertigo. EGb 761® appears to be extremely well tolerated with few side effects and good compliance. The aim of this study is to compare the clinical effectiveness and safety of EGb 761® and betahistine in the treatment of vertigo.

Who can participate?
Male or female outpatients aged 45 or over with vertigo.

What does the study involve?
To determine their eligibility for the study, participants will undergo a physical examination, ECG and laboratory tests (blood sampling at the beginning and end of the study). Participants will then be randomly allocated to receive either EGb 761® or betahistine for 12 weeks. During the study visits participants will complete questionnaires to assess their symptoms.

What are the possible benefits and risks of participating?
According to abundant evidence from other studies and many years of use, there is no major risk linked to the intake of EGb 761® at this dose. The adverse events potentially associated with EGb 761®, such as gastrointestinal symptoms, headache and allergic skin reactions, are usually mild in nature. Bleeding has been observed in individual cases after long-term treatment with Ginkgo preparations, some of unknown origin and quality and in some instances while also being treated with anti-platelet or anti-coagulant drugs. However, specific studies with EGb 761® at

dose levels up to 480 mg per day have shown no effect on coagulation or platelet function. Betahistine may have the following side effects: immune system disorders: hypersensitivity (allergic) reactions (such as anaphylaxis) have been reported; gastrointestinal disorders: in some cases mild gastric complaints have been observed, these can normally be dealt with by taking the dose during meals; skin and subcutaneous tissue disorders: in very rare cases cutaneous hypersensitivity reactions have been reported, in particular angioneurotic oedema (sudden onset of face, neck or limb swelling), urticaria (hives), rash and pruritus (itchiness). There is hardly any risk associated with the tests and examinations required by this study, except for a small risk of infection during blood sample drawing. On the other hand, based on the earlier clinical findings described above it can be expected that patients will benefit from the treatment with EGb 761® or betahistine.

Where is the study run from?
The study is running from ten sites/university-based clinics in Ukraine.

When is the study starting and how long is it expected to run for?
The study ran from September 2011 to September 2012.

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

Who is the main contact?
Mrs Anna Wacker
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Contact information

Type(s)
Scientific

Contact name
Prof L. I. Sokolova

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Additional identifiers

Protocol serial number
523001.01.100

Study information

Scientific Title
Randomized, reference-controlled, double-blind phase III trial to compare the efficacy and safety of Ginkgo biloba extract EGb 761® and betahistine in the treatment of vertigo

Study objectives
The objective of this clinical trial is to compare the clinical efficacy and safety of the Ginkgo biloba special extract EGb 761® and betahistine in the treatment of vertigo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central Ethics Committee, Ministry of Health Ukraine, 16/02/2011

Primary study design
Interventional

Study design
Randomized reference-controlled parallel-group double-blind trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vertigo

Interventions
2x120 mg Ginkgo biloba extract EGb 761® or 2x16 mg betahistine per day for 12 weeks

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ginkgo biloba extract EGb 761®, betahistine

Primary outcome(s)
1. 11-point Numeric Analogue Scale (NAS), measurement of subjectively perceived severity of vertigo
2. Short form of the Vertigo Symptom Scale (VSS-SF), subjectively perceived severity of vertigo symptoms
3. Sheehan Disability Scale (SDS), assessment of the impairment of daily living
4. Clinical Global Impression (CGI), physician rated, for changes from baseline as well as as for the assessment of the tolerability
Measured at screening, baseline (Day 0), Week 4, Week 8 and the final visit Week 12

Key secondary outcome(s)

1. Physical examination
2. Neuro-otological examination
3. Electrocardiogram (ECG)
4. Vital signs
5. Adverse events
5. Laboratory tests
Measured at baseline and end of trial

Completion date
30/09/2012

Eligibility

Key inclusion criteria
1. Diagnosis of vertiginous syndrome not otherwise specified (ICD-10, H 81.9) or peripheral vertigo not otherwise specified (ICD-10, H81.3). (This excludes specific disorders of vestibular function such as Ménière's disease, benign paroxysmal vertigo, vestibular neuronitis, Lermoyez syndrome and central positional nystagmus as well as acute dysfunction of the inner ear)
2. Symptoms of vertigo for at least 3 months
3. At least moderate severity of vertigo, i.e. a score of ≥ 3 on the Numeric Analogue Scale (NAS) at screening
4. Male or female outpatients aged ≥ 45 years
5. Signed Informed consent in accordance with the legal requirements
6. Sufficient language skills, readiness and ability on the part of the patient to comply with the physicians instructions, respond to all interview questions, and to fill in the self-assessment scales without evident difficulties and without the assistance of an interpreter
7. Negative pregnancy test at screening visit in females of childbearing potential (non-childbearing potential is defined as post-menopause for at least one year or surgical sterilization or hysterectomy at least three months before study start)
8. Use of adequate contraception by female with childbearing potential (hormonal: oral, implants, hormonal intrauterine contraceptive device (IUCD); or intrauterine contraception devices)

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 12 weeks before enrolment
2. Treament in the last 12 weeks with Ginkgo-biloba preparations or in the last 8 weeks with any cerebral blood circulation enhancing medications or antiemetics, anti-vertigo agents or

antidementia drugs
3. More than 2 years present therapy-resistant vertigo
4. Morbus Ménière or Lermoyez syndrome
5. Current hospitalization of the patient
6. Contraindication for the treatment with betahistine: pheochromocytoma or bronchial asthma
7. History or evidence of alcohol and/or substance abuse or dependence within the last 5 years
8. Unacceptability to discontinue or likelihood to need medication during the study that is prohibited as concomitant treatment. The following medication is not allowed during the study:
8.1. Any psychotropic drugs including CNS stimulants, tranquilizers / hypnotics (e.g. benzodiazepines, non-benzodiazepine tranquilizers/anyiolytics like zopiclone or zolpidem, barbiturates), neuroleptics / antipsychotics, antidepressants, antiepileptics, antihistaminics and nootropics
8.2. Treatments for neuro-degenerative diseases (e. g. tacrine, donepezil, rivastigmin, metrifonate, galanthamin or any other cholinesterase inhibitor or cholinergic agonist, N-Methyl-D-Aspartate (NMDA)-antagonists (e.g. memantine), nimodipine, vasodilators and haemorheological agents with cerebral activity (e. g. bencyclane, buflomedil, hydergine), other cognition enhancers (e. g. piracetam)
8.3. Anticholinergic and anti-Parkinson drugs (e.g. oxybutynin, tolterodine, trospium chloride, propiverin, l-dopa, selegilin, amantadine, biperiden, benzatropin, metixen etc)
8.4. Anticonvulsants (carbamazepin, phenytoin)
8.5. Antiemetics, anti-vertigo agents
8.6. Aminoglycoside antibiotics
8.7. Long-term therapy with salycilates (> 100mg per day)
8.8. Loop diuretics: furosemide, bumetanide
8.9. Antineoplastics (cisplatin, carboplatin)
8.10. Quinine
9. Clinically significant abnormality of ECG and/or laboratory value(s)
10. Severe, uncontrolled cardiovascular disease, especially:
10.1. Severe (stage IV acc. to the Canadian Cardiovascular Society) or unstable angina pectoris
10.2. Decompensated congestive heart failure [New York Heart Association (NYHA) stage IV]
10.3. Myocardial infarction within the last 6 months
10.4. Uncontrolled hypertension (systolic pressure >180 mmHg, diastolic pressure >115 mmHg)
10.5. Known clinically significant cardiac arrhythmias
10.6. Atrial fibrillation with known or suspected left ventricular myocardial dysfunction.
11. Any severe
11.1. Hepatic, renal disorders [serum creatinine or serum aspartate amino transferase (ASAT), alanine amino transferase (ALAT) or Gamma-glytamyl transpeptidase (Gamma GT)] above 3 times the upper limit of the reference range
11.2. Insulin dependent diabetes mellitus
11.3. Respiratory diseases
11.4. Metabolic disorder or progressive diseases, such as cancer (exception: prostate cancer T1N0M0 which does not require treatment within the next 7 months except hormone therapy)
11.5. Haematologic diseases
11.6. Neurological diseases (epilepsy or a history of seizure disorder or treatment with anticonvulsants for epilepsy or seizures, Parkinsons disease, multiple sclerosis, injury with residual neurologic deficits)
12. Severe head trauma, brain tumor, apoplexy
13. Neuritis vestibularis, herpes zoster oticus
14. Vertigo due to specific somatic diseases, e.g. orthostatic hypotension, hypertension, hematological or metabolical disorders
15. Benign paroxysmal positional vertigo
16. Known hypersensitivity to Ginkgo biloba extract or betahistine dihydrochloride or to any

components of the preparations
17. Gastrointestinal disorders with uncertain absorption of orally administered drugs (e.g. partial or total gastrectomy, enterectomy, inflammatory bowel disease, celiac disease, symptomatic lactose intolerance, other disorders associated with chronic diarrhoea)
18. Pregnancy, lactation

Date of first enrolment
30/09/2011

Date of final enrolment
30/09/2012

Locations

Countries of recruitment
Ukraine

Study participating centre
Bogomolets National Medical University
Kiev
Ukraine
03110

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2014		Yes	No