Clinical trial results:
Monocenter, prospective, randomized placebo-controlled, double blind phase II trial to evaluate protective effects of Gingko biloba extract EGb 761® on temporary hearing damage caused by noise.

Summary

EudraCT number	2013-000614-38
Trial protocol	DE
Global end of trial date	16 September 2016

Results information

Result version number	v1 (current)
This version publication date	28 September 2017
First version publication date	28 September 2017

Trial information

Trial identification

Sponsor protocol code	MW010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. Willmar Schwabe GmbH & Co. KG
Sponsor organisation address	Willmar-Schwabe-Str. 4, Karlsruhe, Germany, 76227
Public contact	Abteilung Medizinische Wissenschaft, Dr. Willmar Schwabe GmbH & Co. KG, +49 07243106573, mw010@schwabe.de
Scientific contact	Abteilung Medizinische Wissenschaft, Dr. Willmar Schwabe GmbH & Co. KG, +49 07243106573, mw010@schwabe.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2016
Global end of trial reached?	Yes
Global end of trial date	16 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy of EGb 761® against temporary hearing impairment due to noise (bilaterally 5 minutes 110 dB broadband noise) in healthy subjects.

Protection of trial subjects:

Safety monitoring (adverse events [AEs], serious adverse events [SAEs], adverse drug reactions [ADRs]), assessment of laboratory data (blood chemistry, hematology), physical examination, ECG and vital signs.

Background therapy:

None

Evidence for comparator:

Not applicable. Placebo-controlled trial; no active comparator was used.

Actual start date of recruitment	02 July 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 202
Worldwide total number of subjects	202
EEA total number of subjects	202

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	202
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

202 subjects were enrolled and randomized. The duration of the recruitment phase was about two years. First subject was enrolled on 02-Jul-2014 (FPFV).

Pre-assignment

Screening details:

Suitable subjects were selected by the investigator according to the eligibility criteria specified in the protocol. 225 subjects were screened. 23 of the subjects were deemed screening failures. 202 subjects were enrolled into the trial.

Pre-assignment period milestones

Number of subjects started	225[1]
Number of subjects completed	202

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Inclusion criteria not met: 12
Reason: Number of subjects	Exclusion criteria not met: 8
Reason: Number of subjects	Not specified: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 225 patients have been screened. 23 patients were deemed screening failures and were considered not eligible for participation. 202 patients were actually enrolled and randomized.

Period 1

Period 1 title	Randomization
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	EGb 761(R)

Arm description:

Randomization | no study drug administration

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Placebo

Arm description:

Randomization | no study drug administration

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	EGb 761(R)	Placebo
Started	100	102
Completed	99	101
Not completed	1	1
Consent withdrawn by subject	-	1
Lost to follow-up	1	-

Period 2	
Period 2 title	Baseline
Is this the baseline period?	Yes[2]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms	
Are arms mutually exclusive?	Yes
Arm title	EGb 761(R)

Arm description:

Baseline | no study drug administration

Arm type	Experimental
Investigational medicinal product name	EGb 761
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

EGb 761 120 mg b.i.d. | p.o.

Arm title	Placebo

Arm description:

Baseline | no study drug administration

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Twice daily one film-coated tablet of placebo matching EGb 761 p.o. for four weeks.

Notes:

[2] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Demographic and baseline characteristics were evaluated prior to randomization. However, a baseline period was set in this database for technical reasons to correctly enter demographic and baseline data, as the number of subjects in "the reporting group" is automatically set and cannot be changed. The reason for this is that the number of subjects for which demographic and baseline data was evaluated was different from the total number of randomized subjects.

Number of subjects in period 2[3]	EGb 761(R)	Placebo
Started	99	101
Completed	99	101

Notes:

[3] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The total number of randomized subjects (n=202) was higher than the number of subjects for which baseline data and demographic data was evaluated (n=200). Demographic and baseline characteristics were only evaluated for subjects included in the safety set (SAF; n=200).

Period 3

Period 3 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	EGb 761(R)

Arm description:

EGb 761(R) 120 mg b.i.d. | p.o.

Arm type	Experimental
Investigational medicinal product name	EGb 761(R)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

EGb 761(R) 120 mg b.i.d. | p.o.

Arm title	Placebo

Arm description:

Placebo matching EGb 761 b.i.d. | p.o.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Twice daily one film-coated tablet of placebo matching EGb 761 p.o. for four weeks.

Number of subjects in period 3	EGb 761(R)	Placebo
Started	99	101
Completed	98	100
Not completed	1	1
Physician decision	1	-
Adverse event, non-fatal	-	1

Period 4	
Period 4 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	EGb 761(R)

Arm description:

Follow-up | no study drug administration

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Placebo

Arm description:

Follow-up | no study drug administration

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	EGb 761(R)	Placebo
Started	98	100
Completed	98	100

Baseline characteristics

Reporting groups	
Reporting group title	EGb 761(R)
Reporting group description: Baseline | no study drug administration	
Reporting group title	Placebo
Reporting group description: Baseline | no study drug administration	

Reporting group values	EGb 761(R)	Placebo	Total
Number of subjects	99	101	200
Age categorical Units: Subjects			
Adults (18-64 years)	99	101	200
Not recorded	0	0	0
Age continuous Units: years			
arithmetic mean	22.2	21.6	
standard deviation	± 1.9	± 2	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	99	101	200
Ethnic origin Units: Subjects			
Asian	1	1	2
Caucasian	97	100	197
Other: Arabic	1	0	1
Height (cm) Units: cm			
arithmetic mean	182.6	182.5	
standard deviation	± 6.9	± 7	-
Weight Units: kg			
arithmetic mean	78.9	79.4	
standard deviation	± 10.5	± 12.8	-
Body Mass Index Units: kg/m^2			
arithmetic mean	23.6	23.7	
standard deviation	± 2.4	± 2.9	-

Subject analysis sets	
Subject analysis set title	EGb 761(R) - FAS
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis	
Subject analysis set title	Placebo - FAS

Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis	
Subject analysis set title	EGb 761(R) - PPS
Subject analysis set type	Per protocol
Subject analysis set description: Per Protocol analysis	
Subject analysis set title	Placebo - PPS
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol analysis	
Subject analysis set title	EGb 761(R) - SAF
Subject analysis set type	Safety analysis
Subject analysis set description: Safety population	
Subject analysis set title	Placebo - SAF
Subject analysis set type	Safety analysis
Subject analysis set description: Safety population	

Reporting group values	EGb 761(R) - FAS	Placebo - FAS	EGb 761(R) - PPS
Number of subjects	98	100	90
Age categorical Units: Subjects			
Adults (18-64 years) Not recorded			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			
Ethnic origin Units: Subjects			
Asian Caucasian Other: Arabic			
Height (cm) Units: cm arithmetic mean standard deviation	±	±	±
Weight Units: kg arithmetic mean standard deviation	±	±	±
Body Mass Index Units: kg/m^2 arithmetic mean standard deviation	±	±	±

Reporting group values	Placebo - PPS	EGb 761(R) - SAF	Placebo - SAF
Number of subjects	88	99	101
Age categorical Units: Subjects			
Adults (18-64 years)		99	101
Not recorded		0	0
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			
Ethnic origin Units: Subjects			
Asian Caucasian Other: Arabic			
Height (cm) Units: cm arithmetic mean standard deviation	±	±	±
Weight Units: kg arithmetic mean standard deviation	±	±	±
Body Mass Index Units: kg/m^2 arithmetic mean standard deviation	±	±	±

End points

End points reporting groups

Reporting group title	EGb 761(R)
Reporting group description: Randomization | no study drug administration	
Reporting group title	Placebo
Reporting group description: Randomization | no study drug administration	
Reporting group title	EGb 761(R)
Reporting group description: Baseline | no study drug administration	
Reporting group title	Placebo
Reporting group description: Baseline | no study drug administration	
Reporting group title	EGb 761(R)
Reporting group description: EGb 761(R) 120 mg b.i.d. | p.o.	
Reporting group title	Placebo
Reporting group description: Placebo matching EGb 761 b.i.d. | p.o.	
Reporting group title	EGb 761(R)
Reporting group description: Follow-up | no study drug administration	
Reporting group title	Placebo
Reporting group description: Follow-up | no study drug administration	
Subject analysis set title	EGb 761(R) - FAS
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis	
Subject analysis set title	Placebo - FAS
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis	
Subject analysis set title	EGb 761(R) - PPS
Subject analysis set type	Per protocol
Subject analysis set description: Per Protocol analysis	
Subject analysis set title	Placebo - PPS
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol analysis	
Subject analysis set title	EGb 761(R) - SAF
Subject analysis set type	Safety analysis
Subject analysis set description: Safety population	
Subject analysis set title	Placebo - SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population

Primary: Average increase in auditory threshold [all frequencies] - FAS

End point title	Average increase in auditory threshold [all frequencies] - FAS

End point description:

FAS Analysis

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	9.9 (± 4.6)	10.3 (± 5.3)		

Statistical analyses

Statistical analysis title	2-sided t-test (all frequencies) - FAS

Statistical analysis description:

Analysis of the FAS: 2-sided t-test to compare the average increase of auditory thresholds over all frequencies of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5923
Method	t-test, 2-sided

Primary: Average increase in auditory threshold [all frequencies] - PPS

End point title	Average increase in auditory threshold [all frequencies] - PPS

End point description:

PPS analysis

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	9.8 (± 4.4)	10.4 (± 5.4)		

Statistical analyses

Statistical analysis title	2-sided t-test (all frequencies) - PPS
Statistical analysis description:	
Analysis of the PPS: 2-sided t-test to compare the average increase of auditory thresholds over all frequencies of subjects receiving EGb 761(R) vs. subjects receiving Placebo.	
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4641
Method	t-test, 2-sided

Primary: Average increase in auditory thresholds over 3, 4, 6 and 8 kHz - FAS

End point title	Average increase in auditory thresholds over 3, 4, 6 and 8 kHz - FAS
End point description:	
Analysis of FAS	
End point type	Primary
End point timeframe:	
Measurements performed after 4-weeks of treatment with study medication (visit 03)	

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: db				
arithmetic mean (standard deviation)	11.9 (± 5.2)	12.8 (± 6.4)		

Statistical analyses

Statistical analysis title	2-sided t-test (3,4,6 and 8 kHz) - FAS
Statistical analysis description:	
Analysis of the FAS | Sensitivity Analysis 1: 2-sided t-test to compare the average increase of auditory thresholds over 3, 4, 6 and 8 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.	

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2661
Method	t-test, 2-sided

Primary: Average increase in auditory thresholds over 3, 4, 6 and 8 kHz - PPS

End point title	Average increase in auditory thresholds over 3, 4, 6 and 8 kHz - PPS

End point description:

Analysis of PPS

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	11.7 (± 5)	12.7 (± 6.4)		

Statistical analyses

Statistical analysis title	2-sided t-test (3,4,6 and 8 kHz) - PPS

Statistical analysis description:

Analysis of the PPS | Sensitivity Analysis 1: 2-sided t-test to compare the average increase of auditory thresholds
over 3, 4, 6 and 8 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2373
Method	t-test, 2-sided

Primary: Average increase in auditory thresholds | ANCOVA - FAS

End point title	Average increase in auditory thresholds	ANCOVA - FAS

End point description:

ANCOVA of average increase in auditory thresholds with treatment as inter-subject factor and time between end of irradiation and start of audiometry after irradiation as covariate.

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: db				
least squares mean (standard error)	9.9846 (± 0.4707)	10.2571 (± 0.466)		

Statistical analyses

Statistical analysis title	ANCOVA - FAS

Statistical analysis description:

Analysis of the FAS:

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.6813
Method	ANCOVA

Notes:

[1] - Treatment df=1; F=0.17; p=0.6813
Audiometry lag [min] df=1; F=26.82; p<0.0001

Primary: Average increase in auditory thresholds | ANCOVA - PPS

End point title	Average increase in auditory thresholds | ANCOVA - PPS

End point description:

ANCOVA of average increase in auditory thresholds with treatment as inter-subject factor and time between end of irradiation and start of audiometry after irradiation as covariate.

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: db				
least squares mean (standard error)	10.0884 (± 0.4748)	10.0733 (± 0.4802)		

Statistical analyses

Statistical analysis title	ANCOVA - PPS

Statistical analysis description:

Analysis of the PPS

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9822 [2]
Method	ANCOVA

Notes:

[2] - Treatment df=1; F=0.00; p=0.9822
Audiometry lag [min] df=1; F=39.44; p<0.0001

Primary: Change in auditory threshold at 3 kHz - FAS

End point title	Change in auditory threshold at 3 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[3]	100		
Units: db				
arithmetic mean (standard deviation)	10 (± 5.6)	10.7 (± 7.7)		

Notes:

[3] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (3 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 3 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4848
Method	t-test, 2-sided

Primary: Change in auditory threshold at 4 kHz - FAS

End point title	Change in auditory threshold at 4 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: db				
arithmetic mean (standard deviation)	14.7 (± 8.8)	15.8 (± 9.6)		

Statistical analyses

Statistical analysis title	Two sided t-test (4 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 4 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4017
Method	t-test, 2-sided

Primary: Change in auditory threshold at 6 kHz - FAS

End point title	Change in auditory threshold at 6 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	12.8 (± 5.4)	14.1 (± 6.3)		

Statistical analyses

Statistical analysis title	Two sided t-test (6 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.1236
Method	t-test, 2-sided

Notes:

[4] - Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 6 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Primary: Change in auditory threshold at 8 kHz - FAS

End point title	Change in auditory threshold at 8 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	9.9 (± 4.8)	10.5 (± 5.7)		

Statistical analyses

Statistical analysis title	Two sided t-test (8 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 8 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4187
Method	t-test, 2-sided

Primary: Change in auditory threshold at 10 kHz - FAS

End point title	Change in auditory threshold at 10 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	8.7 (± 5.1)	7.9 (± 5)		

Statistical analyses

Statistical analysis title	Two sided t-test (10 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 10 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2521
Method	t-test, 2-sided

Primary: Change in auditory threshold at 11.2 kHz - FAS

End point title	Change in auditory threshold at 11.2 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[5]	100		
Units: dB				
arithmetic mean (standard deviation)	7.2 (± 5.8)	6.9 (± 5.7)		

Notes:

[5] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (11.2 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 11.2 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7022
Method	t-test, 2-sided

Primary: Change in auditory threshold at 12.5 kHz - FAS

End point title	Change in auditory threshold at 12.5 kHz - FAS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[6]	100		
Units: dB				
arithmetic mean (standard deviation)	6.2 (± 6.1)	6.3 (± 6.4)		

Notes:

[6] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (12.5 kHz) - FAS

Statistical analysis description:

Analysis of the FAS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 12.5 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9751
Method	t-test, 2-sided

Primary: Change in auditory threshold at 3 kHz - PPS

End point title	Change in auditory threshold at 3 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89[7]	88		
Units: dB				
arithmetic mean (standard deviation)	9.8 (± 5.4)	10.5 (± 7.8)		

Notes:

[7] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (3 kHz) - PPS

Statistical analysis description:

Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 3 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4526
Method	t-test, 2-sided

Primary: Change in auditory threshold at 4 kHz - PPS

End point title	Change in auditory threshold at 4 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	14.2 (± 8.3)	15.7 (± 9.3)		

Statistical analyses

Statistical analysis title	Two sided t-test (4 kHz) - PPS

Statistical analysis description:

Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 4 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2734
Method	t-test, 2-sided

Primary: Change in auditory threshold at 6 kHz - PPS

End point title	Change in auditory threshold at 6 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	12.7 (± 5.3)	14.1 (± 6.3)		

Statistical analyses

Statistical analysis title	Two sided t-test (6 kHz) - PPS
Statistical analysis description:	
Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 6 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.	
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1313
Method	t-test, 2-sided

Primary: Change in auditory threshold at 8 kHz - PPS

End point title	Change in auditory threshold at 8 kHz - PPS
End point description:	
End point type	Primary
End point timeframe:	
Measurements performed after 4-weeks of treatment with study medication (visit 03)	

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	10.1 (± 4.8)	10.6 (± 5.9)		

Statistical analyses

Statistical analysis title	Two sided t-test (8 kHz) - PPS
Statistical analysis description:	
Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 8 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.	
Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5327
Method	t-test, 2-sided

Primary: Change in auditory threshold at 10 kHz - PPS

End point title	Change in auditory threshold at 10 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	8.7 (± 5.1)	7.9 (± 5.2)		

Statistical analyses

Statistical analysis title	Two sided t-test (10 kHz) - PPS

Statistical analysis description:

Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 10 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3362
Method	t-test, 2-sided

Primary: Change in auditory threshold at 11.2 kHz - PPS

End point title	Change in auditory threshold at 11.2 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89[8]	88		
Units: dB				
arithmetic mean (standard deviation)	7.1 (± 5.7)	7.3 (± 5.9)		

Notes:

[8] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (11.2 kHz) - PPS

Statistical analysis description:

Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 11.2 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8692
Method	t-test, 2-sided

Primary: Change in auditory threshold at 12.5 kHz - PPS

End point title	Change in auditory threshold at 12.5 kHz - PPS

End point description:

End point type	Primary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication (visit 03)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89[9]	88		
Units: dB				
arithmetic mean (standard deviation)	6.2 (± 6)	6.5 (± 6.5)		

Notes:

[9] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test (12.5 kHz) - PPS

Statistical analysis description:

Analysis of the PPS| Sensitivity Analysis 2: Two sided t-test to compare the change of auditory thresholds at 12.5 kHz of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7715
Method	t-test, 2-sided

Secondary: Subjects with increase of auditory threshold > 5 dB (3 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (3 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[10]	100		
Units: No. of subjects with increased threshold	2	0		

Notes:

[10] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Fisher Exact Test (3 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2412
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (4 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (4 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: No. of subjects with increased threshold	1	0		

Statistical analyses

Statistical analysis title	Fisher Exact Test (4 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4949
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (6 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (6 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: No. of subjects with increased threshold	1	2		

Statistical analyses

Statistical analysis title	Fisher Exact Test (6 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (8 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (8 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: No. of subjects with increased threshold	4	3		

Statistical analyses

Statistical analysis title	Fisher Exact Test (8 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7195
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (10 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (10 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: No. of subjects with increased threshold	5	4		

Statistical analyses

Statistical analysis title	Fisher Exact Test (10 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7463
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (11.2 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (11.2 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[11]	100		
Units: No. of subjects with increased threshold	9	5		

Notes:

[11] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Fisher Exact Test (11.2 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS

Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.278
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (12.5 kHz) - FAS

End point title	Subjects with increase of auditory threshold > 5 dB (12.5 kHz) - FAS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97[12]	100		
Units: No. of subjects with increased threshold	9	8		

Notes:

[12] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Fisher Exact Test (12.5 kHz) - FAS
Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8037
Method	Fisher exact

Secondary: Decrease of the DPOAE (V4-V3pre) - FAS

End point title	Decrease of the DPOAE (V4-V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[13]	99[14]		
Units: dB				
arithmetic mean (standard deviation)	0.2 (± 1.5)	-0.1 (± 1.9)		

Notes:

[13] - Data for two subjects missing.

[14] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2714
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post - V3pre) - FAS

End point title	Decrease of the DPOAE (V3post - V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	99[15]		
Units: dB				
arithmetic mean (standard deviation)	-2.1 (± 2.1)	-2.2 (± 2)		

Notes:

[15] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V3post-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7052
Method	t-test, 2-sided

Secondary: Decrease of the TEOAE (V4-V3pre) - FAS

End point title	Decrease of the TEOAE (V4-V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-0.4 (± 1.7)	-0.2 (± 1.3)		

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE (V4-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of TEOAE from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3392
Method	t-test, 2-sided

Secondary: Decrease of the TEOAE (V3post - V3pre) - FAS

End point title	Decrease of the TEOAE (V3post - V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-1.6 (± 3.4)	-2 (± 4)		

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE (V3post-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of TEOAE at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5442
Method	t-test, 2-sided

Secondary: Decrease of TEOAE suppression (V4-V3pre) - FAS

End point title	Decrease of TEOAE suppression (V4-V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	99[16]		
Units: dB				
arithmetic mean (standard deviation)	-0.3 (± 1.6)	-0.1 (± 1.7)		

Notes:

[16] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE suppress. (V4-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE suppression from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5679
Method	t-test, 2-sided

Secondary: Decrease of TEOAE suppression (V3post - V3pre) - FAS

End point title	Decrease of TEOAE suppression (V3post - V3pre) - FAS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	99[17]		
Units: dB				
arithmetic mean (standard deviation)	-0.4 (± 3.6)	-0.5 (± 4.2)		

Notes:

[17] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE suppr. (V3post-V3pre) - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of TEOAE suppression at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS

Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8136
Method	t-test, 2-sided

Secondary: Subjects with increase of auditory threshold > 5 dB (3 kHz) - PPS

End point title	Subjects with increase of auditory threshold > 5 dB (3 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89[18]	88		
Units: No. of subjects with increased threshold	2	0		

Notes:

[18] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Fisher Exact Test (3 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4972
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (4 kHz) - PPS

End point title	Subjects with increase of auditory threshold > 5 dB (4 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: No. of subjects with increased threshold	1	0		

Statistical analyses

Statistical analysis title	Fisher Exact Test (4 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (6 kHz) - PPS	
End point title	Subjects with increase of auditory threshold > 5 dB (6 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: No. of subjects with increased threshold	1	2		

Statistical analyses

Statistical analysis title	Fisher Exact Test (6 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6186
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (8 kHz) - PPS

End point title	Subjects with increase of auditory threshold > 5 dB (8 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: No. of subjects with increased threshold	3	3		

Statistical analyses

Statistical analysis title	Fisher Exact Test (8 kHz) -PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (10 kHz) - PPS

End point title	Subjects with increase of auditory threshold > 5 dB (10 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: No. of subjects with increased threshold	4	4		

Statistical analyses

Statistical analysis title	Fisher Exact Test (10 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (11.2 kHz) - PPS	
End point title	Subjects with increase of auditory threshold > 5 dB (11.2 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: No. of subjects with increased threshold	8	5		

Statistical analyses

Statistical analysis title	Fisher Exact Test (11.2 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5662
Method	Fisher exact

Secondary: Subjects with increase of auditory threshold > 5 dB (12.5 kHz) - PPS

End point title	Subjects with increase of auditory threshold > 5 dB (12.5 kHz) - PPS

End point description:

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04)

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	89[19]	88		
Units: No. of subjects with increased threshold	8	7		

Notes:

[19] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Fisher Exact Test (12.5 kHz) - PPS
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Decrease of the DPOAE (V4-V3pre) - PPS

End point title	Decrease of the DPOAE (V4-V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[20]	87[21]		
Units: dB				
arithmetic mean (standard deviation)	0.1 (± 1.6)	-0.1 (± 2)		

Notes:

[20] - Data for two subjects missing.

[21] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761 vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3326
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post - V3pre) - PPS

End point title	Decrease of the DPOAE (V3post - V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-2.1 (± 2.1)	-2.2 (± 2)		

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V3post-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761 vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7454
Method	t-test, 2-sided

Secondary: Decrease of the TEOAE (V4-V3pre) - PPS

End point title	Decrease of the TEOAE (V4-V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-0.4 (± 1.8)	-0.3 (± 1.3)		

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE (V4-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of TEOAE from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761 vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6945
Method	t-test, 2-sided

Secondary: Decrease of the TEOAE (V3post - V3pre) - PPS

End point title	Decrease of the TEOAE (V3post - V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-1.7 (± 3.5)	-1.7 (± 3.1)		

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE (V3post-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of TEOAE at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8556
Method	t-test, 2-sided

Secondary: Decrease of TEOAE suppression (V4-V3pre) - PPS

End point title	Decrease of TEOAE suppression (V4-V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	87[22]		
Units: dB				
arithmetic mean (standard deviation)	-0.2 (± 1.7)	-0.3 (± 1.6)		

Notes:

[22] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE suppress. (V4-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE suppression from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8686
Method	t-test, 2-sided

Secondary: Decrease of TEOAE suppression (V3post - V3pre) - PPS

End point title	Decrease of TEOAE suppression (V3post - V3pre) - PPS

End point description:

Results display decrease observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	87[23]		
Units: dB				
arithmetic mean (standard deviation)	-0.4 (± 3.8)	-0.3 (± 3.8)		

Notes:

[23] - Data for one subject missing.

Statistical analyses

Statistical analysis title	Two sided t-test TEOAE suppr. (V3post-V3pre) - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of TEOAE suppression at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9032
Method	t-test, 2-sided

Secondary: DPOAE Growth Function - FAS

End point title	DPOAE Growth Function - FAS

End point description:

DPOAE growth function at 4004 Hz, Signal-to-noise ratio (SNR) measured at 5 predefined sound level pairs.

End point type	Secondary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication prior (visit 03-pre) and after (visit 03-post) accoustic Irradiation.

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	95		
Units: dB				
least squares mean (standard error)	8.0261 (± 0.3805)	7.6022 (± 0.3726)		

Statistical analyses

Statistical analysis title	ANCOVA DPOAE Growth Function (SNR) - FAS

Statistical analysis description:

Analysis of the FAS: ANCOVA of DPOAE growth function (at 4 kHz) taking into account measured levels of eliciting sounds, irradiation, time lag since irradiation, body side, and treatment group to compare differences between changes in SNR after acoustic irradiation of subjects receiving EGb 761(R) vs . Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0104 [24]
Method	ANCOVA

Notes:

[24] - p-value for interaction timepoint (pre vs. post irradiation) x treatment

Secondary: DPOAE Growth Function - PPS

End point title	DPOAE Growth Function - PPS

End point description:

DPOAE growth function at 4004 Hz, Signal-to-noise ratio (SNR) measured at 5 predefined sound level pairs

End point type	Secondary

End point timeframe:

Measurements performed after 4-weeks of treatment with study medication prior (visit 03-pre) and after (visit 03-post) accoustic Irradiation.

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	83	84		
Units: dB				
least squares mean (standard error)	8.4504 (± 0.4007)	7.4385 (± 0.3987)		

Statistical analyses

Statistical analysis title	ANCOVA DPOAE Growth Function (SNR) - PPS

Statistical analysis description:

Analysis of the PPS: ANCOVA of DPOAE growth function (at 4 kHz) taking into account measured levels of eliciting sounds, irradiation, time lag since irradiation, body side, and treatment group to compare differences between changes in SNR after acoustic irradiation of subjects receiving EGb 761(R) vs . Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0245 [25]
Method	ANCOVA

Notes:

[25] - p-value for interaction timepoint (pre vs. post irradiation) x treatment

Secondary: Decrease of the DPOAE (V4-V3pre) | 1.0 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre)	1.0 kHz - FAS

End point description:

Results display decrease measured at 1.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[26]	100		
Units: dB				
arithmetic mean (standard deviation)	-0.3 (± 4.1)	-0.8 (± 5.2)		

Notes:

[26] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 1.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5027
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 1.4 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre) | 1.4 kHz - FAS

End point description:

Results display decrease measured at 1.4 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[27]	100		
Units: dB				
arithmetic mean (standard deviation)	0.7 (± 3.8)	-0.1 (± 4.8)		

Notes:

[27] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 1.4 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.4 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving

Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2113
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 2.0 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre) | 2.0 kHz - FAS

End point description:

Results display decrease measured at 2.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[28]	100		
Units: dB				
arithmetic mean (standard deviation)	0.6 (± 3.7)	-0.4 (± 4.1)		

Notes:

[28] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 2.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0685
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 2.8 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre) | 2.8 kHz - FAS

End point description:

Results display decrease measured at 2.8 kHz observed four weeks after treatment discontinuation (visit

04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[29]	100		
Units: dB				
arithmetic mean (standard deviation)	0 (± 3)	0 (± 4.3)		

Notes:

[29] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 2.8 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.8 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.935
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 4.0 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre) | 4.0 kHz - FAS

End point description:

Results display decrease measured at 4.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[30]	100		
Units: dB				
arithmetic mean (standard deviation)	0.3 (± 3.1)	-0.3 (± 3.2)		

Notes:

[30] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 4.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 4.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2061
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 6.0 kHz - FAS

End point title	Decrease of the DPOAE (V4-V3pre) | 6.0 kHz - FAS

End point description:

Results display decrease measured at 6.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96[31]	100		
Units: dB				
arithmetic mean (standard deviation)	0.5 (± 2.8)	0.2 (± 3.7)		

Notes:

[31] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 6.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 6.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving

Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5657
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 1.0 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 1.0 kHz - FAS

End point description:

Results display decrease measured at 1.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-2.1 (± 4.2)	-1.7 (± 3.4)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 1.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4471
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 1.4 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 1.4 kHz - FAS

End point description:

Results display decrease measured at 1.4 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-1.4 (± 3.5)	-1.5 (± 5)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 1.4 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.4 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9261
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 2.0 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 2.0 kHz - FAS

End point description:

Results display decrease measured at 2.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-1.5 (± 3.7)	-2.1 (± 3.3)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 2.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2475
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 2.8 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 2.8 kHz - FAS

End point description:

Results display decrease measured at 2.8 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-2.4 (± 3.5)	-2.5 (± 4.3)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 2.8 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.8 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8236
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 4.0 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 4.0 kHz - FAS

End point description:

Results display decrease measured at 4.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-4.4 (± 5)	-6.1 (± 7.2)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 4.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 4.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0544
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 6.0 kHz - FAS

End point title	Decrease of the DPOAE (V3post-V3pre) | 6.0 kHz - FAS

End point description:

Results display decrease measured at 6.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic
irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	100		
Units: dB				
arithmetic mean (standard deviation)	-5.5 (± 4.6)	-5.1 (± 5.1)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 6.0 kHz - FAS

Statistical analysis description:

Analysis of the FAS| Two sided t-test to compare changes in decrease of DPOAE measured at 6.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - FAS v Placebo - FAS
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.559
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 1.0 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 1.0 kHz - PPS

End point description:

Results display decrease measured at 1.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88	88[32]		
Units: dB				
arithmetic mean (standard deviation)	-0.2 (± 4.2)	-0.6 (± 5.2)		

Notes:

[32] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 1.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5861
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 1.4 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 1.4 kHz - PPS

End point description:

Results display decrease measured at 1.4 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[33]	88		
Units: dB				
arithmetic mean (standard deviation)	0.7 (± 3.9)	-0.2 (± 5)		

Notes:

[33] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 1.4 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.4 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1721
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 2.0 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 2.0 kHz - PPS

End point description:

Results display decrease measured at 2.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[34]	88		
Units: dB				
arithmetic mean (standard deviation)	0.6 (± 3.8)	-0.5 (± 4.3)		

Notes:

[34] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 2.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0683
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 2.8 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 2.8 kHz - PPS

End point description:

Results display decrease measured at 2.8 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[35]	88		
Units: dB				
arithmetic mean (standard deviation)	0 (± 3)	0 (± 4.3)		

Notes:

[35] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 2.8 kHz - PPS

Statistical analysis description:

Analysis of thePPS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.8 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9919
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 4.0 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 4.0 kHz - PPS

End point description:

Results display decrease measured at 4.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[36]	88		
Units: dB				
arithmetic mean (standard deviation)	0.3 (± 3.2)	-0.2 (± 3.2)		

Notes:

[36] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 4.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 4.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3572
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V4-V3pre) | 6.0 kHz - PPS

End point title	Decrease of the DPOAE (V4-V3pre) | 6.0 kHz - PPS

End point description:

Results display decrease measured at 6.0 kHz observed four weeks after treatment discontinuation (visit 04) compared to values recorded four weeks after treatment Initiation prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment and 4 weeks of follow-up (visit 04).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	88[37]	88		
Units: dB				
arithmetic mean (standard deviation)	0.5 (± 2.8)	0.1 (± 3.7)		

Notes:

[37] - Data for two subjects missing.

Statistical analyses

Statistical analysis title	Two sided t-test DPOAE (V4-V3pre) | 6.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 6.0 kHz from V3 (prior to acoustic Irradiation) to V4 of subjects receiving EGb 761(R) vs. subjects receiving Placebo

Comparison groups	EGb 761(R) - PPS v Placebo - PPS

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4432
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 1.0 kHz - PPS

End point title	Decrease of the DPOAE (V3post-V3pre) | 1.0 kHz - PPS

End point description:

Results display decrease measured at 1.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-2.3 (± 4.3)	-1.6 (± 3.3)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 1.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2238
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 1.4 kHz - PPS

End point title	Decrease of the DPOAE (V3post-V3pre) | 1.4 kHz - PPS

End point description:

Results display decrease measured at 1.4 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-1.5 (± 3.5)	-1.4 (± 4.1)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 1.4 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 1.4 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8761
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 2.0 kHz - PPS

End point title	Decrease of the DPOAE (V3post-V3pre) | 2.0 kHz - PPS

End point description:

Results display decrease measured at 2.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-1.6 (± 3.8)	-2.2 (± 3.3)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 2.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	Placebo - PPS v EGb 761(R) - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2789
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 2.8 kHz - PPS

End point title	Decrease of the DPOAE (V3post-V3pre) | 2.8 kHz - PPS

End point description:

Results display decrease measured at 2.8 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).

End point type	Secondary

End point timeframe:

Measurements were performed after 4 weeks of treatment (visit 03).

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-2.5 (± 3.5)	-2.6 (± 4)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 2.8 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 2.8 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8756
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 4.0 kHz - PPS	
End point title	Decrease of the DPOAE (V3post-V3pre) | 4.0 kHz - PPS
End point description:	
Results display decrease measured at 4.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).	
End point type	Secondary
End point timeframe:	
Measurements were performed after 4 weeks of treatment (visit 03).	

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-4.1 (± 4.8)	-5.8 (± 6.9)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 4.0 kHz - PPS
Statistical analysis description:	
Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 4.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.	
Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0627
Method	t-test, 2-sided

Secondary: Decrease of the DPOAE (V3post-V3pre) | 6.0 kHz - PPS	
End point title	Decrease of the DPOAE (V3post-V3pre) | 6.0 kHz - PPS
End point description:	
Results display decrease measured at 6.0 kHz observed four weeks after treatment initiation (visit 03-post) after accoustic irradiation compared to values prior to acoustic irradiation (visit 03-pre).	
End point type	Secondary
End point timeframe:	
Measurements were performed after 4 weeks of treatment (visit 03).	

End point values	EGb 761(R) - PPS	Placebo - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	90	88		
Units: dB				
arithmetic mean (standard deviation)	-5.3 (± 4.4)	-4.8 (± 4.8)		

Statistical analyses

Statistical analysis title	2-sided t-test DPOAE (V3post-V3pre)| 6.0 kHz - PPS

Statistical analysis description:

Analysis of the PPS| Two sided t-test to compare changes in decrease of DPOAE measured at 6.0 kHz at V3 prior to acoustic Irradiation and after acoustic Irradiation of subjects receiving EGb 761(R) vs. subjects receiving Placebo.

Comparison groups	EGb 761(R) - PPS v Placebo - PPS
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4664
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events (AEs) were reported during the entire study course.	
Adverse event reporting additional description:	
AEs reported prior to first administration of study medication were reported as medical history. AEs reported after administration of study medication were defined as treatment emergent.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	EGb 761(R) - SAF
Reporting group description:	
EGb 761(R) 120 mg b.i.d. | p.o.	
Reporting group title	Placebo - SAF
Reporting group description:	
Placebo matching EGb 761 b.i.d. | p.o.	

Serious adverse events	EGb 761(R) - SAF	Placebo - SAF	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 99 (1.01%)	0 / 101 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 99 (1.01%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	EGb 761(R) - SAF	Placebo - SAF	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 99 (9.09%)	6 / 101 (5.94%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 99 (9.09%)	6 / 101 (5.94%)	
occurrences (all)	10	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 May 2014	The protocol had to be changed as the actual technical conditions of the measuring apparatus were different from the conditions specified in the protocol. All changes made to the protocol were approved according to local law (GCP-V §10 (1)).
18 December 2014	Changes to the protocol were related to secondary endpoints (TEOAEs and DPOAEs) due to technical requirements. All changes made to the protocol were approved according to local law (GCP-V §10 (1))

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported