Clinical trial results:
Randomised, double-blind trial to compare the treatment effects of Ginkgo biloba extract EGb 761® and pentoxifylline in patients with sub-chronic and chronic tinnitus focussing on psycho-social problems

Summary

EudraCT number	2011-004697-28
Trial protocol	CZ
Global end of trial date	22 August 2013

Results information

Result version number	v1 (current)
This version publication date	01 March 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	523001.01.099

Additional study identifiers

ISRCTN number	ISRCTN68772788
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. W. Schwabe GmbH & Co. KG
Sponsor organisation address	Willmar Schwabe Str. 4, Karlsruhe, Germany, 76227
Public contact	Clinical Research Department, Dr. W. Schwabe GmbH & Co. KG, +49 72140058573,
Scientific contact	Clinical Research Department, Dr. W. Schwabe GmbH & Co. KG, +49 7214005573,

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	05 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 August 2013
Global end of trial reached?	Yes
Global end of trial date	22 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the treatment effects of Ginkgo biloba extract EGb 761® and pentoxifylline in patients with sub-chronic or chronic tinnitus focussing on psycho-social problems

Protection of trial subjects:

Possibility to withdraw consent by patient. Monitoring of adverse events and laboratory parameters.

Background therapy: -

Evidence for comparator:

Pentoxifylline improves haemorrheology and tissue perfusion by increasing red blood cell deformability and decreasing blood viscosity. It inhibits the aggregation of red blood cells and thrombocytes and decreases plasma fibrinogen levels. Pentoxifylline also inhibits the activation of leucocytes and their adhesion to the endothelium. The drug is registered and frequently prescribed to treat disorders of the inner ear that are related to impaired perfusion.

Actual start date of recruitment	13 September 2012
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	Czech Republic: 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)	164
From 65 to 84 years	38

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 202 patients were screened for inclusion into the trial. Two patients were not randomized and did not receive the investigational product since they terminated the trial before randomization and dispensation of the investigational product.

Pre-assignment period milestones

Number of subjects started	202
Number of subjects completed	200

Pre-assignment subject non-completion reasons

Reason: Number of subjects	lost to follow-up: 2

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	EGb 761®

Arm description:

Film-coated tablets containing 120 mg of Gingko biloba special extract EGb 761® (SMC: 5560) and pentoxifylline-placebo tablets (SMC: 9076P).
One patient was randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period and did not undergo at least 42 days of observation. The patient was excluded from the FAS.

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:

One tablet in the morning and one tablet in the evening for 12 consecutive weeks. Each tablet contains 120 mg of Gingko biloba special extract EGb 761®.

Investigational medicinal product name	Pentoxifylline-placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet pentoxifylline-placebo in the morning and one tablet pentoxifylline-placebo in the evening for 12 consecutive weeks. The tablet pentoxifylline-placebo and the film-coated EGb 761® tablet were to be

swallowed as a whole with some liquid.

Arm title	Pentoxifylline

Arm description:

Extended-release tablets containing 600 mg of pentoxifylline (SMC: 9076) and EGb 761®-placebo film-coated tables (SMC: 5560P).
Two patients were randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period. One of those two patients did not undergo at least 42 days of observation and the other patient did not show a compliance between 80% and 120% for the first 42 days of observation. Both patients were excluded from the FAS.

Arm type	Active comparator
Investigational medicinal product name	Pentoxifylline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet in the morning and one tablet in the evening for 12 consecutive weeks. Each tablet contains 600 mg of pentoxifylline.

Investigational medicinal product name	EGb 761®-placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet EGb 761®-placebo in the morning and one tablet EGb 761®-placebo in the evening for 12 consecutive weeks. The tablet EGb 761®-placebo and the extended release pentoxifylline tablet were to be swallowed as a whole with some liquid.

Number of subjects in period 1[1]	EGb 761®	Pentoxifylline
Started	100	100
Completed	93	83
Not completed	7	17
Consent withdrawn by subject	-	1
Physician decision	-	1
Adverse event, non-fatal	6	14
Private reasons	1	-
Lost to follow-up	-	1

Notes:

[1] - 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: In total, 2 of the 202 subjects screened for inclusion into the trial were not included into the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	EGb 761®

Reporting group description:

Film-coated tablets containing 120 mg of Gingko biloba special extract EGb 761® (SMC: 5560) and pentoxifylline-placebo tablets (SMC: 9076P).
One patient was randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period and did not undergo at least 42 days of observation. The patient was excluded from the FAS.

Reporting group title	Pentoxifylline

Reporting group description:

Extended-release tablets containing 600 mg of pentoxifylline (SMC: 9076) and EGb 761®-placebo film-coated tables (SMC: 5560P).
Two patients were randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period. One of those two patients did not undergo at least 42 days of observation and the other patient did not show a compliance between 80% and 120% for the first 42 days of observation. Both patients were excluded from the FAS.

Reporting group values	EGb 761®	Pentoxifylline	Total
Number of subjects	100	100	200
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	77	85	162
From 65-84 years	23	15	38
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.3	53	
standard deviation	± 10.48	± 10.84	-
Gender categorical Units: Subjects			
Female	41	39	80
Male	59	61	120

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full analysis set (FAS) included all subjects who received an investigational product at least once and had at least one post-baseline measurement of one of the 11-Point Box Scales.
Subjects that dropped out after dispensation of the investigational product without measurements of the 11-Point Box Scales for both parameters during the randomised treatment period and intake of the investigational product at least once were included in the FAS if they had at least 42 days of observation, a compliance between 80% and 120% for this period and at least one of the following conditions was met for the reason of drop out:
1) "Lack of efficacy" or "Unexpected improvement/ remission of disease relevant for trial indication" or
2) "Adverse event" and a causal relationship of the AE with the investigational product was not excluded (causal relationship assessed as "unlikely", "possible" or "probable")

Reporting group values	Full analysis set		
Number of subjects	197		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	159		
From 65-84 years	38		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	54.3		
standard deviation	± 10.75		
Gender categorical Units: Subjects			
Female	80		
Male	117		

End points

End points reporting groups

Reporting group title	EGb 761®

Reporting group description:

Film-coated tablets containing 120 mg of Gingko biloba special extract EGb 761® (SMC: 5560) and pentoxifylline-placebo tablets (SMC: 9076P).
One patient was randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period and did not undergo at least 42 days of observation. The patient was excluded from the FAS.

Reporting group title	Pentoxifylline

Reporting group description:

Extended-release tablets containing 600 mg of pentoxifylline (SMC: 9076) and EGb 761®-placebo film-coated tables (SMC: 5560P).
Two patients were randomized and started treatment but had no post-baseline measurements of the 11-Point Box Scales during the randomized 12-week treatment period. One of those two patients did not undergo at least 42 days of observation and the other patient did not show a compliance between 80% and 120% for the first 42 days of observation. Both patients were excluded from the FAS.

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full analysis set (FAS) included all subjects who received an investigational product at least once and had at least one post-baseline measurement of one of the 11-Point Box Scales.
Subjects that dropped out after dispensation of the investigational product without measurements of the 11-Point Box Scales for both parameters during the randomised treatment period and intake of the investigational product at least once were included in the FAS if they had at least 42 days of observation, a compliance between 80% and 120% for this period and at least one of the following conditions was met for the reason of drop out:
1) “Lack of efficacy" or “Unexpected improvement/ remission of disease relevant for trial indication” or
2) “Adverse event" and a causal relationship of the AE with the investigational product was not excluded (causal relationship assessed as "unlikely", "possible" or "probable")

Primary: Change in 11-Point Box Scales for tinnitus loudness between baseline and end of treatment

End point title	Change in 11-Point Box Scales for tinnitus loudness between baseline and end of treatment

End point description:

The 11-Point Box Scales for tinnitus loudness and annoyance were assessed at each day during the trial. The evaluation of the scales was based on mean weekly values per subject. The baseline value was determined by calculating the mean of all documented assessments from the screening visit onwards (including) until randomization.

Note: No formal hypotheses were formulated, there was no formal differentiation between primary and secondary end points and data were analyzed descriptively. The effectiveness of EGb 761® in comparison to pentoxifylline was described primarily using the changes of the 11-point box scales for tinnitus loudness and annoyance and the changes of the Mini-TQ total score during the 12 weeks of treatment.

End point type	Primary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	98		
Units: points				
arithmetic mean (standard deviation)	-0.4 (± 1.34)	-0.45 (± 1.3)		

Statistical analyses

Statistical analysis title	ANCOVA
Statistical analysis description:	
ANCOVA with factor treatment and the respective baseline score as covariate, LOCF method was used	
Comparison groups	EGb 761® v Pentoxifylline
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other[1]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.39

Notes:

[1] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Primary: Change in 11-Point Box Scales for tinnitus annoyance between baseline and end of treatment

End point title	Change in 11-Point Box Scales for tinnitus annoyance between baseline and end of treatment

End point description:

The 11-Point Box Scales for tinnitus loudness and annoyance were assessed at each day during the trial. The evaluation of the scales was based on mean weekly values per subject. The baseline value was determined by calculating the mean of all documented assessments from the screening visit onwards (including) until randomization.

Note: No formal hypotheses were formulated, there was no formal differentiation between primary and secondary end points and data were analyzed descriptively. The effectiveness of EGb 761® in comparison to pentoxifylline was described primarily using the changes of the 11-point box scales for tinnitus loudness and annoyance and the changes of the Mini-TQ total score during the 12 weeks of treatment.

End point type	Primary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	98		
Units: points				
arithmetic mean (standard deviation)	-0.54 (± 1.48)	-0.56 (± 1.4)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

ANCOVA with factor treatment and respective baseline score as covariate, LOCF method was used.

Comparison groups	EGb 761® v Pentoxifylline
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	other[2]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.39

Notes:

[2] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Primary: Change in Abridged Tinnitus Questionnaire (Mini-TQ) between baseline and end of treatment

End point title	Change in Abridged Tinnitus Questionnaire (Mini-TQ) between baseline and end of treatment

End point description:

The abridged Tinnitus Questionnaire (Mini-TQ) includes 12 items with questions related to the subjective perception of coping attitudes and beliefs about tinnitus. Each item of the questionnaire is to be rated on a 3-point scale (2=true, 1=partly true, 0=not true).

The maximum score is 24 points with higher scores indicating more severe distress.

Note: No formal hypotheses were formulated, there was no formal differentiation between primary and secondary end points and data were analyzed descriptively. The effectiveness of EGb 761® in comparison to pentoxifylline was described primarily using the changes of the 11-point box scales for tinnitus loudness and annoyance and the changes of the Mini-TQ total score during the 12 weeks of treatment.

End point type	Primary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	90		
Units: Points				
arithmetic mean (standard deviation)	-1.55 (± 3.06)	-1.97 (± 3.73)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

ANCOVA with factor treatment and respective baseline score as covariate, LOCF method was used.

Comparison groups	EGb 761® v Pentoxifylline
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other[3]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.35

Notes:

[3] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Secondary: Change in anxiety score of Hospital Anxiety and Depression Scale (HADS) between baseline and end of treatment

End point title	Change in anxiety score of Hospital Anxiety and Depression Scale (HADS) between baseline and end of treatment

End point description:

The HADS contains of 14 questions, of which seven each are assigned to anxiety and to depression. The answers to each question are rated on a scale from 0 to 3, with higher scores corresponding to a higher degree of anxiety or depression.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	90		
Units: points				
arithmetic mean (confidence interval 95%)	-1.3 (-1.82 to -0.85)	-1.1 (-1.55 to -0.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in depression score of Hospital Anxiety and Depression Scale (HADS) between baseline and end of treatment

End point title	Change in depression score of Hospital Anxiety and Depression Scale (HADS) between baseline and end of treatment

End point description:

The HADS contains of 14 questions, of which seven each are assigned to anxiety and to depression. The answers to each question are rated on a scale from 0 to 3, with higher scores corresponding to a higher degree of anxiety or depression.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	90		
Units: Points				
arithmetic mean (confidence interval 95%)	-0.4 (-0.89 to 0.15)	-0.5 (-0.92 to 0.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in global impairment score of the Sheehan Disability Score (SDS) between baseline and end of treatment

End point title	Change in global impairment score of the Sheehan Disability Score (SDS) between baseline and end of treatment

End point description:

The Sheehan Disability Scale is a brief self-report (patient-rated) inventory. All items are scored on a 0-10 scale, where 0 represents no impairment, 1-3 mild impairment, 4-6 moderate impairment, 7-9 marked impairment and 10 extreme impairment.
A total score named “global impairment” is calculated as the sum of the first three items of the questionnaire.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	90		
Units: Points				
arithmetic mean (standard deviation)	-1.67 (± 4.9)	-1.88 (± 5.41)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

ANCOVA with factor treatment and respective score as covariate, LOCF method was used

Comparison groups	EGb 761® v Pentoxifylline
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[4]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	1.02

Notes:

[4] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Secondary: Change of Item 4 score of the Sheehan Disability Scale (SDS)

End point title	Change of Item 4 score of the Sheehan Disability Scale (SDS)

End point description:

Number of days lost in the last week (with regard to missed school or work or unable to carry out normal daily responsibilities)

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	90		
Units: Points				
arithmetic mean (standard deviation)	0.01 (± 0.23)	-0.07 (± 0.95)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

ANCOVA with factor treatment and respective baseline score as covariate, LOCF method was used

Comparison groups	Pentoxifylline v EGb 761®
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other[5]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.12

Notes:

[5] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Secondary: Change of Item 5 score of the Sheehan Disability Scale (SDS)

End point title	Change of Item 5 score of the Sheehan Disability Scale (SDS)

End point description:

Number of days with reduced productivity (with regard to school, work)

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	90		
Units: Points				
arithmetic mean (standard deviation)	-0.32 (± 1.51)	-0.22 (± 1.8)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

ANCOVA with factor treatment and respective baseline score as covariate, LOCF method was used

Comparison groups	EGb 761® v Pentoxifylline
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	other[6]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.11

Notes:

[6] - The confidence intervals of differences of LS means were computed to compare the effectiveness of the treatments.
Difference EGb 761® - Pentoxifylline was calculated.

Secondary: Speech audiometry: percentage of words comprehended with sound level 60 dB with the right ear

End point title	Speech audiometry: percentage of words comprehended with sound level 60 dB with the right ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	1.6 (-1.27 to 4.5)	1.9 (-0.47 to 4.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Speech audiometry: percentage of words comprehended with sound level 60 dB with the left ear

End point title	Speech audiometry: percentage of words comprehended with sound level 60 dB with the left ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	0.2 (-1.97 to 2.29)	-0.6 (-2.21 to 1.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Speech audiometry: percentage of words comprehended with sound level 80 dB with the right ear

End point title	Speech audiometry: percentage of words comprehended with sound level 80 dB with the right ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	1.4 (-0.65 to 3.45)	1.4 (-1.26 to 4.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Speech audiometry: percentage of words comprehended with sound level 80 dB with the left ear

End point title	Speech audiometry: percentage of words comprehended with sound level 80 dB with the left ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	2.1 (0.09 to 4.1)	0 (-0.76 to 0.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Speech audiometry: percentage of words comprehended with sound level 100 dB with the right ear

End point title	Speech audiometry: percentage of words comprehended with sound level 100 dB with the right ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words

comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	-0.3 (-4.02 to 3.38)	3.4 (-0.27 to 7.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Speech audiometry: percentage of words comprehended with sound level 100 dB with the left ear

End point title	Speech audiometry: percentage of words comprehended with sound level 100 dB with the left ear

End point description:

The change between baseline and end of treatment was evaluated for the percentage of words comprehended.

Note: Mean changes (+95%-CIs) from baseline to week 12 for EGb 761® and pentoxifylline were used to compare the two treatments descriptively.

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (12-week treatment period)

End point values	EGb 761®	Pentoxifylline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	83		
Units: Percentage				
arithmetic mean (confidence interval 95%)	0.1 (-3.17 to 3.38)	2.1 (-1.59 to 5.81)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information
Timeframe for reporting adverse events:
12 weeks + 2 days
Adverse event reporting additional description:
During the active treatment and subsequent risk phase 19/100 (19.0%) subjects from the EGb 761® group experienced a total of 20 AEs leading to an overall incidence rate of 0.0024 AEs/day of exposure. In the pentoxifylline group 27/100 (27.0%) subjects experienced a total of 36 AEs leading to an overall incidence rate of 0.0048 AEs/day of exposure.

Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	PENTOXIFYLLINE
Reporting group description:	
Active comparator	
Reporting group title	EGb 761
Reporting group description:	
Active treatment	
Reporting group title	No active treatment
Reporting group description:	
No active treatment	

Serious adverse events	PENTOXIFYLLINE	EGb 761	No active treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	0 / 200 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	PENTOXIFYLLINE	EGb 761	No active treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 100 (3.00%)	5 / 100 (5.00%)	0 / 200 (0.00%)
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 100 (3.00%)	5 / 100 (5.00%)	0 / 200 (0.00%)
occurrences (all)	3	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 July 2012	The trial schedule was changed because due to organisational reasons the start of patients´ recruitment had to be adjusted. Inclusion criterion 1 was changed to allow the enrolment of subjects aged between 30 and 40 years in addition. Exclusion criterion "12 Alcohol or substance addiction or abuse (i.e. consumption at higher quantities or frequencies than generally socially accepted) within the last 10 years" was added. In the section describing forbidden concomitant therapy the use of anti-epileptic drugs was added. The patient information and informed consent form (Final version from 08 March 2012) had been linguistically revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported