Clinical trial results:
Efficacy and safety of a fixed combination of cinnarizine 20 mg and dimenhydrinate 40 mg vs betahistine dihydrochloride 16 mg in patients with vertigo of peripheral origin. A multi-centre, double-blind, randomised, active-controlled, stratified two-parallel group clinical study

Summary

EudraCT number	2011-004025-27
Trial protocol	AT CZ BG
Global end of trial date	14 April 2015

Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020

Trial information

Trial identification

Sponsor protocol code	Antivert1-B09_PE_V1.0

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hennig Arzneimittel GmbH & Co. KG
Sponsor organisation address	Liebigstrasse 1-2, Flörsheim am Main, Germany,
Public contact	Clinical Trials Information, HENNIG ARZNEIMITTEL GmbH & Co. KG, +49 61455080,
Scientific contact	Clinical Trials Information, HENNIG ARZNEIMITTEL GmbH & Co. KG, +49 61455080,

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	21 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2015
Global end of trial reached?	Yes
Global end of trial date	14 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to demonstrate that the antivertiginous efficacy of the fixed combination cinnarizine/dimenhydrinate is non-inferior to betahistine dihydrochloride 16 mg in patients suffering from vertigo of peripheral origin.

Protection of trial subjects:

No specific measures were taken other than good clinical practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2013
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	Austria: 100
Country: Number of subjects enrolled	Bulgaria: 103
Country: Number of subjects enrolled	Czech Republic: 63
Country: Number of subjects enrolled	Russian Federation: 40
Worldwide total number of subjects	306
EEA total number of subjects	266

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)	229
From 65 to 84 years	76

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Male and female outpatients (age ≥ 18 years) suffering from peripheral vestibular vertigo related to various origins were recruited. All patients gave their written informed consent prior to enrollment in the study. The first patient was included in the clinical study on 24 July 2013, the last patient finished the study on 14 April 2015.

Pre-assignment

Screening details:

362 patients were assessed for eligibility (screening), of which 306 patients were included in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cinnarizine/Dimenhydrinate

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Arlevert
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 times 1 tablet per day

Arm title	Betahistine

Arm description: -

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

Dosage and administration details:

3 times 1 tablet per day

Number of subjects in period 1	Cinnarizine/Dimenhydrinate	Betahistine
Started	152	154
Completed	149	148
Not completed	3	6
Consent withdrawn by subject	-	1
Adverse event, non-fatal	2	5
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cinnarizine/Dimenhydrinate
Reporting group description: -	
Reporting group title	Betahistine
Reporting group description: -	

Reporting group values	Cinnarizine/Dimenhydrinate	Betahistine	Total
Number of subjects	152	154	306
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)	115	114	229
From 65-84 years	37	39	76
85 years and over	0	1	1
Gender categorical Units: Subjects			
Female	94	90	184
Male	58	64	122

End points

End points reporting groups

Reporting group title	Cinnarizine/Dimenhydrinate
Reporting group description: -	
Reporting group title	Betahistine
Reporting group description: -	

Primary: Change in Mean Vertigo Score (MVS) between baseline and end of treatment (4 weeks)

End point title	Change in Mean Vertigo Score (MVS) between baseline and end of treatment (4 weeks)
End point description:	
12-item composite score of 6 (unprovoked) vertigo symptoms and vertigo in consequence of 6 triggering factors	
End point type	Primary
End point timeframe:	
4 weeks treatment	

End point values	Cinnarizine/Dimenhydrinate	Betahistine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	148		
Units: Mean Vertigo Score				
least squares mean (confidence interval 95%)	0.395 (0.333 to 0.456)	0.488 (0.472 to 0.550)		

Statistical analyses

Statistical analysis title	ANCOVA on MVS reduction
Comparison groups	Cinnarizine/Dimenhydrinate v Betahistine
Number of subjects included in analysis	294
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.035
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.093
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.007
upper limit	0.18

Notes:
[1] - Non-inferiority margin set to 0.3

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During study treatment (4 weeks)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	Cinnarizine/Dimenhydrinate
Reporting group description: -	
Reporting group title	Betahistine
Reporting group description: -	

Serious adverse events	Cinnarizine/Dimenhydrinate	Betahistine	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 152 (0.00%)	0 / 154 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Cinnarizine/Dimenhydrinate	Betahistine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 152 (2.63%)	8 / 154 (5.19%)	
Investigations			
blood pressure increased			
subjects affected / exposed	0 / 152 (0.00%)	1 / 154 (0.65%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 152 (0.66%)	0 / 154 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
allergic reaction			

subjects affected / exposed occurrences (all)	1 / 152 (0.66%) 1	1 / 154 (0.65%) 1	
Ear and labyrinth disorders vertigo attack subjects affected / exposed occurrences (all)	 0 / 152 (0.00%) 0	 4 / 154 (2.60%) 4	
Gastrointestinal disorders dry mouth subjects affected / exposed occurrences (all)	 1 / 152 (0.66%) 1	 1 / 154 (0.65%) 1	
Skin and subcutaneous tissue disorders worsening of seborroeic dermatitis subjects affected / exposed occurrences (all)	 1 / 152 (0.66%) 1	 0 / 154 (0.00%) 0	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	 1 / 152 (0.66%) 1	 0 / 154 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31571128