Clinical trial results:
Effect of gabapentine as symptomatic therapy for cerebellar ataxia in degenerative and inflammatory CNS-disease

Summary

EudraCT number	2008-005167-33
Trial protocol	DE
Global end of trial date	31 March 2016

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	1210

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité University Medicine Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Dr. Sarah Doss, Clinic for Neurology with Experimental Neurology, +49 030 450 560117, sarahjmdoss@gmail.com
Scientific contact	Dr. Sarah Doss, Clinic for Neurology with Experimental Neurology, +49 030 450 560117, sarah.doss@charite.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	31 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Effect of gabapentine versus placebo on ataxia after 7 weeks of treatment measured with cllinical ataxia rating scale (SARA)

Protection of trial subjects:

The dosage was slowly increased to insure that the individual dosage for each patient is correct. Further to reduce the dosage if negativ efficay occurs.

Background therapy:

Patients with cerebellar ataxia with coordination deficits in walking, upper and lower limb movements and oculomtoor coordination deficits are included in the trial.
The cause of their atayia is either a degenerative CNS disease such as autosomal dominant Spinocerebellar Ataxia or sporadic ataxia with late onset or inflammatory CNS disease (Multiple Sclerosis).

Evidence for comparator: -	
Actual start date of recruitment	02 August 2010
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: 71
Worldwide total number of subjects	71
EEA total number of subjects	71

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)	71

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited by the Ataxie-Ambulance and the residing neurologists at Charité - Universitätsmedizin Berlin

Pre-assignment

Screening details:

72 Patients were recruited. 1 was excluded due to laboratory deviations. The recruitment was nation wide.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Gabapentine Arm

Arm description:

Between day 1 and day 21 the total dosage was between 600-1800mg a day. Totatel dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safty and to adjust the dosage if side affect occurs.

Arm type	Experimental
Investigational medicinal product name	gabapentine
Investigational medicinal product code	GBP
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Each capsule was 300mg. The subjects received 600-1800mg each day, distributed on three daily doses.

Arm title	Placebo Arm

Arm description:

The placebo was administered the same way as the investigational drug gabapentin.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Ocular use

Dosage and administration details:

Each capsule is 300mg. 600-1800mg a day. Distributed in three daily doses

Number of subjects in period 1	Gabapentine Arm	Placebo Arm
Started	36	35
Completed	29	29
Not completed	7	6
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	1
no specified reasons	2	2
Protocol deviation	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Gabapentine Arm
Reporting group description:	
Between day 1 and day 21 the total dosage was between 600-1800mg a day. Totatel dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safty and to adjust the dosage if side affect occurs.	
Reporting group title	Placebo Arm
Reporting group description:	
The placebo was administered the same way as the investigational drug gabapentin.	

Reporting group values	Gabapentine Arm	Placebo Arm	Total
Number of subjects	36	35	71
Age categorical Units: Subjects			
Adults 18-75	36	35	71
Age continuous Units: years			
arithmetic mean	53.47	49.72	
standard deviation	± 12.06	± 13.66	-
Gender categorical Units: Subjects			
Female	19	23	42
Male	17	12	29
SARA score			
Scale for the assessment and rating of ataxia (SARA)			
Units: Score			
median	10	9.5	
standard deviation	± 7.11	± 6.28	-
CCFS			
Cerebellar Composite Functional Score (CCFS)			
Units: Score			
median	1.07	1.11	
standard deviation	± 0.21	± 0.14	-
UHDRS IV			
Unified Huntington's Disease Rating Scale (UHDRS) part IV			
Units: Score			
median	20	21	
standard deviation	± 5.47	± 4.17	-

End points

End points reporting groups

Reporting group title	Gabapentine Arm
Reporting group description:	
Between day 1 and day 21 the total dosage was between 600-1800mg a day. Totatel dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safty and to adjust the dosage if side affect occurs.	
Reporting group title	Placebo Arm
Reporting group description:	
The placebo was administered the same way as the investigational drug gabapentin.	

Primary: Change SARA-Score Verum vs. Placebo from V1 to V3

End point title	Change SARA-Score Verum vs. Placebo from V1 to V3
End point description:	
End point type	Primary
End point timeframe:	
from 0 up to 7 weeks	

End point values	Gabapentine Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: score				
median (standard deviation)	10.5 (± 7.71)	9.5 (± 6.14)		

Attachments (see zip file)	Change SARA-Score_V1-V2-V33/Att2_Change in SARA-Score

Statistical analyses

Statistical analysis title	Mann-Whitney
Statistical analysis description:	
Since the data were not normally distributed, the assessment for significance was performed for the related variables using the Wilcoxon test and for the unrelated variables using the Mann-Whitney U test as non-parametric tests. Significance was assumed at a probability of error of $p \leq 0.05$.	
Comparison groups	Gabapentine Arm v Placebo Arm

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - The difference in SARA difference between the first and third visit of cases and control group was found to be not significant by Mann-Whitney U test (U=335.50; Z= -1.327; p=0.185).

Secondary: change in UHDRS part IV between V1and V3

End point title	change in UHDRS part IV between V1and V3

End point description:

End point type	Secondary

End point timeframe:

from 0 up to 7 weeks

End point values	Gabapentine Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	29		
Units: score				
median (standard deviation)	18.72 (± 5.694)	20.39 (± 4.5)		

Attachments (see zip file)	Change in UHDRS_V1-V3/Att1_Change in UHDRS _V1-V3.pdf

Statistical analyses

Statistical analysis title	Mann-Whitney
Comparison groups	Gabapentine Arm v Placebo Arm
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.5 [2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - The difference in UHDRS difference between the first and third visit of cases and control group was found to be not significant by Mann-Whitney U test (U=381.500; Z= -0.421; p=0.674); Verum (Z= -0.353, p= 0.370) and placebo (Z= 0.00, p=0.537)

Secondary: Change CCFS of total cohort

End point title	Change CCFS of total cohort

End point description:

End point type	Secondary

End point timeframe:

from V1 to V3

End point values	Gabapentine Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: score				
median (standard error)	1.12 (± 0.199)	1.07 (± 0.148)		

Statistical analyses

Statistical analysis title	Mann-Whitney
Comparison groups	Placebo Arm v Gabapentine Arm
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.5 [3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - The difference in CCFS between V1 to V3 significant by Mann-Whitney U test (U=336.00; Z= -0.77; p=0.480). There was no significant difference in change of CCFS in Verum group (Z= -0.072, p= 0.943) and placebo group (Z= -0.934, p= 0.35).

Secondary: Change in measure SARA of total Cohort V1-V2

End point title	Change in measure SARA of total Cohort V1-V2

End point description:

End point type	Secondary

End point timeframe:

from V1 to V2

End point values	Gabapentine Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: score				
median (standard error)	-0.00 (± 1.82)	-0.75 (± 1.75)		

Attachments (see zip file)	Change SARA-Score_V1-V2-V33/Att2_Change in SARA-Score

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 to Day 49	
Assessment type	Systematic
Dictionary used	
Dictionary name	own
Dictionary version	1
Reporting groups	
Reporting group title	Visitation 2 Verum
Reporting group description: -	
Reporting group title	Visitation 2 Placebo
Reporting group description: -	
Reporting group title	Visitation 3 Verum
Reporting group description: -	
Reporting group title	Visitation 3 Placebo
Reporting group description: -	

Serious adverse events	Visitation 2 Verum	Visitation 2 Placebo	Visitation 3 Verum
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	0 / 35 (0.00%)	0 / 36 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Visitation 3 Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Visitation 2 Verum	Visitation 2 Placebo	Visitation 3 Verum
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 36 (50.00%)	10 / 35 (28.57%)	8 / 36 (22.22%)
Investigations			

Fatigue			
subjects affected / exposed	5 / 36 (13.89%)	3 / 35 (8.57%)	3 / 36 (8.33%)
occurrences (all)	5	3	3
Nervous system disorders			
increased Ataxie			
subjects affected / exposed	3 / 36 (8.33%)	0 / 35 (0.00%)	2 / 36 (5.56%)
occurrences (all)	3	0	2
decreased fine motor skills			
subjects affected / exposed	1 / 36 (2.78%)	0 / 35 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Gait deviation			
subjects affected / exposed	3 / 36 (8.33%)	0 / 35 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Dizziness			
subjects affected / exposed	9 / 36 (25.00%)	5 / 35 (14.29%)	3 / 36 (8.33%)
occurrences (all)	9	5	3
Gastrointestinal disorders			
Constipation, abdomen, Nausea			
subjects affected / exposed	5 / 36 (13.89%)	3 / 35 (8.57%)	0 / 36 (0.00%)
occurrences (all)	5	3	0

Non-serious adverse events	Visitation 3 Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 35 (8.57%)		
Investigations			
Fatigue			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Nervous system disorders			
increased Ataxie			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
decreased fine motor skills			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Gait deviation			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Ear and labyrinth disorders Dizziness subjects affected / exposed occurrences (all)	 2 / 35 (5.71%) 2		
Gastrointestinal disorders Constipation, abdomen, Nausea subjects affected / exposed occurrences (all)	 0 / 35 (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