



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 clinical 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 efficacy occurs.

Background therapy:

Patients with cerebellar ataxia with coordination deficits in walking, upper and lower limb movements and oculomotor coordination deficits are included in the trial.

The cause of their ataxia 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. Total dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safety 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. Total dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safety 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. Total dosage was below the recommended max. dosage of 3600mg a day. Further, the medication was increased slowly to insure the patients safety 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 occurrences (all) | 5 / 36 (13.89%) 5 | 3 / 35 (8.57%) 3 | 3 / 36 (8.33%) 3 |
| Nervous system disorders increased Ataxie subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | 0 / 35 (0.00%) 0 | 2 / 36 (5.56%) 2 |
| decreased fine motor skills subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 35 (0.00%) 0 | 2 / 36 (5.56%) 2 |
| Gait deviation subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | 0 / 35 (0.00%) 0 | 0 / 36 (0.00%) 0 |
| Ear and labyrinth disorders Dizziness subjects affected / exposed occurrences (all) | 9 / 36 (25.00%) 9 | 5 / 35 (14.29%) 5 | 3 / 36 (8.33%) 3 |
| Gastrointestinal disorders Constipation, abdomen, Nausea subjects affected / exposed occurrences (all) | 5 / 36 (13.89%) 5 | 3 / 35 (8.57%) 3 | 0 / 36 (0.00%) 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 occurrences (all) | 2 / 35 (5.71%) 2 | | |
| Nervous system disorders increased Ataxie subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | | |
| decreased fine motor skills subjects affected / exposed occurrences (all) | 1 / 35 (2.86%) 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