



Clinical trial results:

A double-blind, placebo-controlled, dose-ranging clinical study to evaluate the safety, tolerability, and antiepileptic activity of ganaxolone in treatment of patients with infantile spasms.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-004285-13 |
| Trial protocol | CZ |
| Global end of trial date | 08 May 2008 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 17 June 2022 |
| First version publication date | 17 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 1042-0500 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00441896 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Marinus Pharmaceuticals, Inc. |
| Sponsor organisation address | 5 Radnor Corporate Center 100 Matsonford Rd, Suite 500 , Radnor, United States, 19087 |
| Public contact | Regulatory Affairs, Marinus Pharmaceuticals, Inc., regulatory@marinuspharma.com |
| Scientific contact | Regulatory Affairs, Marinus Pharmaceuticals, Inc., regulatory@marinuspharma.com |

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 | 08 August 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 May 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 May 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and antiepileptic activity of variable ascending doses of ganaxolone and to determine the therapeutic dose of ganaxolone in subjects (ages 4 to 24 months) with infantile spasms (IS).

Protection of trial subjects:

At the first visit, prior to initiation of any study-related procedures, the parent(s) or legal guardian(s) of the subjects gave their written consent to participate in the study after having been informed about the nature and purpose of the study, participation / termination conditions, and risks and benefits. Before the informed consent document was signed, the investigator, or a person designated by the investigator, provided the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial were answered to the satisfaction of the subject or the subject's legally acceptable representative.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 23 February 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 3 |
| Country: Number of subjects enrolled | Czechia: 3 |
| Country: Number of subjects enrolled | Romania: 2 |
| Country: Number of subjects enrolled | United States: 36 |
| Country: Number of subjects enrolled | India: 13 |
| Worldwide total number of subjects | 57 |
| EEA total number of subjects | 8 |

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) | 56 |
| Children (2-11 years) | 1 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Treatment-naïve and previously treated patients could enter the study.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 57 |
| Number of subjects completed | 57 |

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 |

Arms

Are arms mutually exclusive? Yes

Arm title Treatment Sequence B

Arm description:

Placebo followed by placebo + ganaxolone

| | |
|--|--------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Ganaxolone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The investigational product was administered as an oral suspension and was administered through an oral dosing syringe by hospital staff/parents/guardians tid, following the morning, noon, and evening feedings. Each dose was separated by a minimum of 4 hours and a maximum of 8 hours.

| | |
|--|--------------------------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

A placebo suspension, which was identical in taste and appearance, was supplied at an equal volume.

Arm title Treatment Sequence A

Arm description:

Ganaxolone followed by ganaxolone + placebo

Arm type Experimental

No investigational medicinal product assigned in this arm

| Number of subjects in period 1 | Treatment Sequence B | Treatment Sequence A |
|---------------------------------------|-------------------------|-------------------------|
| Started | 19 | 38 |
| Completed | 18 | 37 |
| Not completed | 1 | 1 |
| Consent withdrawn by subject | 1 | - |
| Other reasons | - | 1 |

Baseline characteristics

End points

End points reporting groups

| | |
|---|----------------------|
| Reporting group title | Treatment Sequence B |
| Reporting group description: | |
| Placebo followed by placebo + ganaxolone | |
| Reporting group title | Treatment Sequence A |
| Reporting group description: | |
| Ganaxolone followed by ganaxolone + placebo | |

Primary: Spasm frequency

| | |
|---|-----------------|
| End point title | Spasm frequency |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| The spasm frequency was measured from 24-hour vEEG at Visit 2 (baseline), Visit 5 (Day 9 ± 1 day) and Visit 8 (Day 18 ± 2 days) | |

| End point values | Treatment Sequence B | Treatment Sequence A | | |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 37 | | |
| Units: number of spasms in 24 hours | 10 | 10 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Analysis of covariance |
| Statistical analysis description: | |
| The primary efficacy variable was the spasm frequency as measured from 24-hour vEEG at Visit 5 (Day 9 ± 1 day). Comparison between investigational product and placebo on the spasm frequency at Visit 5 was performed by analysis of covariance (ANCOVA) with treatment (active vs. placebo) as the fixed effect and baseline spasm frequency as the covariate. | |
| Comparison groups | Treatment Sequence A v Treatment Sequence B |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.7191 |
| Method | ANCOVA |

Notes:

[1] - p-Value from ANCOVA analysis with treatment sequence as fixed effect and baseline spasm frequency as the covariate.

A paired t-test compared the mean frequency at Visit 5 to the mean frequency at Visit 2.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the finalisation of the entire study.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-----|
| Dictionary version | 9.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Treatment Sequence B |
|-----------------------|----------------------|

Reporting group description:

Placebo followed by placebo + ganaxolone

| | |
|-----------------------|----------------------|
| Reporting group title | Treatment Sequence A |
|-----------------------|----------------------|

Reporting group description:

Ganaxolone followed by ganaxolone + placebo

| Serious adverse events | Treatment Sequence B | Treatment Sequence A | |
|---|----------------------|----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 3 / 37 (8.11%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocephalus | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 37 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Treatment Sequence B | Treatment Sequence A | |
|---|-------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 19 (47.37%) | 25 / 37 (67.57%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 4 / 37 (10.81%) | |
| occurrences (all) | 1 | 4 | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 3 / 37 (8.11%) | |
| occurrences (all) | 0 | 3 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 2 / 37 (5.41%) | |
| occurrences (all) | 2 | 2 | |
| Irritability | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 3 / 37 (8.11%) | |
| occurrences (all) | 0 | 3 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 5 / 37 (13.51%) | |
| occurrences (all) | 2 | 5 | |
| Teething | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 3 / 37 (8.11%) | |
| occurrences (all) | 1 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 4 / 37 (10.81%) | |
| occurrences (all) | 1 | 4 | |
| Infections and infestations | | | |

| | | | |
|---|----------------------|---------------------|--|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 2 | 1 / 37 (2.70%) 1 | |
|---|----------------------|---------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 February 2007 | <ul style="list-style-type: none">- Addition of "Study Drug Administration" at Visits 3, 4, 5, 6, 7, 8 to Table 2.1 Schedule of Events- Removal of requirement for EEG evaluations in diagnosis of IS- Change in procedure to dispose of partially used drug containers from disposal at the study site to return to sponsor |
| 17 April 2007 | Clarification of study procedures regarding rescue medication |
| 31 August 2007 | <ul style="list-style-type: none">- Change in study procedures- Clarification in the numbering of study subjects- Provision of additional information about rescue benzodiazepine |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported