



Clinical trial results:

An open-label clinical study to evaluate the safety and antiepileptic activity of ganaxolone in treatment of patients diagnosed with infantile spasms.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-004286-33 |
| Trial protocol | CZ PL |
| Global end of trial date | 13 March 2009 |

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 | 1042-0501 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00442104 |
| 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 | 13 July 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 March 2009 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 March 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and antiepileptic activity of long-term treatment with ganaxolone in subjects with Infantile spasms (IS) who have completed the double blind controlled trial (Protocol 1042-0500).

Protection of trial subjects:

The study was conducted in accordance with GCP as described in the US CFR, the International Conference on Harmonization, and the ethical principles of the Declaration of Helsinki.

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 and termination conditions, and risks and benefits.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 14 March 2007 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

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: 35 |
| Country: Number of subjects enrolled | India: 11 |
| Worldwide total number of subjects | 54 |
| 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) | 53 |
| 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:

Eligible subjects were infants with IS who completed Protocol 1042-0500 and were deemed eligible by the investigator (had a response to treatment and no SAEs thought to be drug related).

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|--------------------------------|
| Arm title | open label extension |
| Arm description: - | |
| Arm type | Experimental |
| 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:

Open-label dosing commenced at the dose from parent study (Protocol 042-0500) and could be adjusted to optimize efficacy and tolerability (maximum dose: 54 mg/kg/day).

| | |
|---|----------------------|
| Number of subjects in period 1 | open label extension |
| Started | 54 |
| Completed | 7 |
| Not completed | 47 |
| termination of the study by the sponsor | 47 |

Baseline characteristics

End points

End points reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | open label extension |
|-----------------------|----------------------|

Reporting group description: -

Primary: Spasm-free subjects

| | |
|-----------------|------------------------------------|
| End point title | Spasm-free subjects ^[1] |
|-----------------|------------------------------------|

End point description:

Proportion of subjects who were free of spasms at Week 96.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 96

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary efficacy analysis of the proportion of subjects who were free of spasms at Week 96 could not be performed because no subjects completed to Week 96.

| End point values | open label extension | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 7 | | | |
| Units: subjects | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Spasm frequency

| | |
|-----------------|-----------------|
| End point title | Spasm frequency |
|-----------------|-----------------|

End point description:

Frequency of spasm clusters during the last 2 days of each visit period as recorded in the Seizure Diary Summary.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

each visit

| End point values | open label extension | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 49 | | | |
| Units: spasm clusters | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from study start (week 0) up to end of study (week 96)

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Ganaxolone |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events | Ganaxolone | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 54 (44.44%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Infantile spasms | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Convulsion in childhood | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cough | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory distress | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Failure to thrive | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oral intake reduced | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Ganaxolone | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 47 / 54 (87.04%) | | |
| Investigations | | | |
| Hemoglobin decreased | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Convulsion in childhood | | | |
| subjects affected / exposed | 9 / 54 (16.67%) | | |
| occurrences (all) | 9 | | |
| Somnolence | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 7 | | |
| Infantile spasms | | | |
| subjects affected / exposed | 6 / 54 (11.11%) | | |
| occurrences (all) | 6 | | |
| Tonic convulsion | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 4 | | |
| Lethargy | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Irritability subjects affected / exposed occurrences (all) | 26 / 54 (48.15%) 26 6 / 54 (11.11%) 6 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all) gastroesophageal reflux disease subjects affected / exposed occurrences (all) | 15 / 54 (27.78%) 15 8 / 54 (14.81%) 8 7 / 54 (12.96%) 7 7 / 54 (12.96%) 7 6 / 54 (11.11%) 6 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) | 19 / 54 (35.19%) 19 11 / 54 (20.37%) 11 | | |

| | | | |
|--|------------------------|--|--|
| Pneumonia aspiration subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 18 / 54 (33.33%) 18 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 13 / 54 (24.07%) 13 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 8 / 54 (14.81%) 8 | | |
| Ear infection subjects affected / exposed occurrences (all) | 5 / 54 (9.26%) 5 | | |
| Influenza subjects affected / exposed occurrences (all) | 5 / 54 (9.26%) 5 | | |
| Rhinitis subjects affected / exposed occurrences (all) | 5 / 54 (9.26%) 5 | | |
| Bronchitis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Otitis media subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|-----------------------------|----------------|--|--|
| Dehydration | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences (all) | 5 | | |
| Oral intake reduced | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 4 | | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 19 February 2007 | To clarify the need for vEEG to ascertain an infantile spasm diagnosis and to make administrative changes. |
| 17 April 2007 | To add information about the use of rescue benzodiazepines (up to 2 doses in any 7-day period) and to state that 24-hour vEEG was to be performed without benzodiazepines and at least 24 hours after the last benzodiazepine administration. |
| 31 August 2007 | To adjust the planned number of sites and subjects based on enrollment in Protocol 1042-0500, to adjust the schedule of events to give investigators the option of de-escalating ganaxolone over 4 weeks rather than 2 weeks, to clarify the position on the use of benzodiazepines as rescue medication, and to add PK analyses. |
| 27 September 2007 | To increase the duration of treatment from 9 months to 1 year (and therefore add 2 visits to the study schedule) and to clarify that 24-hour vEEG to confirm freedom from spasms was only to be performed if the subject has been free of spasms for 24 hours. |
| 18 January 2008 | To extend the study duration from up to 1 year to 72 weeks (plus a 2- to 4-week taper period), to add 2 more visits to the study schedule to accommodate the increased duration, to change the length of spasm-free time required for a 24-hour vEEG to be performed (from 24 hours to 14 days), and to remove the final vEEG to confirm freedom from spasms if a subject discontinued early due to lack of efficacy. |
| 16 May 2008 | To extend the study duration from 72 weeks to 96 weeks (plus a 2- to 4-week taper period), to add an additional study visit to accommodate the increased duration, to delete cessation of hypsarrhythmia as a secondary endpoint, to update the definition of responder, to delete analysis based on seizure type, and to specify that efficacy analysis at Visit 6 (Week 26) can determine whether there is a clinically significant response to ganaxolone to justify prolonged chronic treatment. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the early closure of the study by the sponsor, the primary efficacy analysis could not be performed.

Notes: