Clinical trial results:
An open-label clinical study to evaluate the safety and antiepileptic activity of ganaxolaone 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 infonned 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	3 / 54 (5.56%)		
occurrences (all)	3		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	26 / 54 (48.15%)		
occurrences (all)	26		
Irritability			
subjects affected / exposed	6 / 54 (11.11%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	15 / 54 (27.78%)		
occurrences (all)	15		
Diarrhoea			
subjects affected / exposed	8 / 54 (14.81%)		
occurrences (all)	8		
Constipation			
subjects affected / exposed	7 / 54 (12.96%)		
occurrences (all)	7		
Teething			
subjects affected / exposed	7 / 54 (12.96%)		
occurrences (all)	7		
gastroesophageal reflux disease			
subjects affected / exposed	6 / 54 (11.11%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 54 (35.19%)		
occurrences (all)	19		
Nasal congestion			
subjects affected / exposed	11 / 54 (20.37%)		
occurrences (all)	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) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Ear infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Otitis media subjects affected / exposed occurrences (all)	18 / 54 (33.33%) 18 13 / 54 (24.07%) 13 8 / 54 (14.81%) 8 5 / 54 (9.26%) 5 5 / 54 (9.26%) 5 5 / 54 (9.26%) 5 3 / 54 (5.56%) 3 3 / 54 (5.56%) 3 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 hypsarrythmia 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: