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-naive 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	- 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	- 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