Clinical trial results:
A controlled double-blind crossover trial of ganaxolone in children with fragile X syndrome

Summary

EudraCT number	2014-000251-89
Trial protocol	BE
Global end of trial date	15 November 2015

Results information

Result version number	v1 (current)
This version publication date	04 September 2021
First version publication date	04 September 2021
Summary attachment (see zip file)	Trial results publication (Ganaxolone.pdf)

Trial information

Trial identification

Sponsor protocol code	1042-0800

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01725152
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Marinus Pharmaceuticals
Sponsor organisation address	100 Matsonford Rd, Radnor, United States,
Public contact	Cognitive Genetics Group, Antwerp University Hospital, +32 32759756, medische.genetica@uza.be
Scientific contact	Cognitive Genetics Group, Antwerp University Hospital, +32 32759756, medische.genetica@uza.be

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	16 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 October 2015
Global end of trial reached?	Yes
Global end of trial date	15 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety, tolerability and efficacy of ganaxolone for treatment of anxiety and attention in subjects with fragile X syndrome.

Protection of trial subjects:

All families signed an informed consent that was reviewed by the UCD Institutional Review Boards (IRBs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2012
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	Belgium: 11
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	59
EEA total number of subjects	11

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)	29
Adolescents (12-17 years)	30
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were selected from existing contacts and though patient organisations. Potential participants were screened by telephone using a questionnaire. Those who met all criteria were scheduled for a baseline visit. All families signed an informed consent that was review ed by the UCD Institutional Review Boards.

Pre-assignment

Screening details:

Baseline assessments included intelligence testing , Autism Diagnostic Observation Schedule (ADOS); Diagnostic and Statistical Manual of Mental Disorders, Text Revision IV (DSM-IV) checklist; and Clinical Global ImpressionSeverity (CGI-S)).

Pre-assignment period milestones

Number of subjects started	59
Number of subjects completed	59

Period 1

Period 1 title	Arm 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

Drugs and placebo were identical and the code was only known to the pharmacist.

Arms

Are arms mutually exclusive?	Yes
Arm title	Drug - Placebo

Arm description:

2-armed trial with cross-over (drug/placebo): first treatment with drug, second with placebo

Arm type	Experimental
Investigational medicinal product name	ganaxolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

3 mg/kg up to 12 mg/kg, with maximum of 1500 mg/day

Arm title	Placebo - Drug

Arm description:

2-armed trial with cross-over (drug/placebo): first treatment with placebo, second with drug

Arm type	Placebo
Investigational medicinal product name	ganaxolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:
3 mg/kg up to 12 mg/kg, with maximum of 1500 mg/day

Number of subjects in period 1	Drug - Placebo	Placebo - Drug
Started	30	29
Completed	25	26
Not completed	5	3
study medication compromised	-	1
Adverse event, non-fatal	4	1
No perceived benefit	-	1
Lost to follow-up	1	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	Drug - Placebo
Reporting group description:	
2-armed trial with cross-over (drug/placebo): first treatment with drug, second with placebo	
Reporting group title	Placebo - Drug
Reporting group description:	
2-armed trial with cross-over (drug/placebo): first treatment with placebo, second with drug	

Primary: Primary end point

End point title	Primary end point
End point description:	
Clinical Global Impression-Improvement (CGI-I) scale was used as primary end point	
End point type	Primary
End point timeframe:	
Measured at the end of each treatment arm	

End point values	Drug - Placebo	Placebo - Drug		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: 3.4-3.5				
least squares mean (standard error)	3.4 (± 0.13)	3.5 (± 0.13)		

Statistical analyses

Statistical analysis title	Linear mixed-effect (LME) model
Statistical analysis description:	
Efficacy was assessed via a linear mixed-effect (LME) model for repeated measures in a ganaxolone/placebo, 2-period crossover trial with primary endpoint at the end of the period.	
Comparison groups	Drug - Placebo v Placebo - Drug
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Mixed models analysis

Notes:

[1] - LMEM

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
After the finalisation of the entire study.	
Adverse event reporting additional description:	
334 adverse events were reported. The top three types of adverse event were upper respiratory infection, fatigue, and drowsiness.	
Assessment type	Systematic

Dictionary used	
Dictionary name	GP
Dictionary version	1

Reporting groups	
Reporting group title	Drug - Placebo
Reporting group description:	
first treatment with drug, second with placebo	
Reporting group title	Placebo - Drug
Reporting group description:	
first treatment with placebo, second with drug	

Serious adverse events	Drug - Placebo	Placebo - Drug	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Drug - Placebo	Placebo - Drug	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 30 (13.33%)	1 / 29 (3.45%)	
Nervous system disorders			
Fatigue	Additional description: Transient fatigue		
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
upper respiratory infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders Rash / Itchiness subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1	 1 / 29 (3.45%) 1	
Psychiatric disorders Aggresion/Agitation subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1	 0 / 29 (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

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

None

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28764646