Clinical trial results:
Double-blind study in paediatric epileptic subjects aged from 5 to less than 8 years to compare the subject preference for ESL suspension formulation with alternative flavours

Summary

EudraCT number	2012-003137-41
Trial protocol	SK
Global end of trial date	31 December 2012

Results information

Result version number	v1 (current)
This version publication date	16 March 2016
First version publication date	16 March 2016

Trial information

Trial identification

Sponsor protocol code	BIA-2093-212

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02021461
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BIAL - Portela & CA, S.A.
Sponsor organisation address	À Av. Siderurgia Nacional, Coronado, Portugal, 4745-457
Public contact	André Garrido, BIAL - Portela & Cª, S.A., 00351 229866100, andre.garrido@bial.com
Scientific contact	José Francisco Rocha, BIAL - Portela & Cª, S.A., 00351 229866100, jose.rocha@bial.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000696-PIP02-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2012
Global end of trial reached?	Yes
Global end of trial date	31 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the taste preference in children for 3 different flavours of the ESL oral suspension.

Protection of trial subjects:

The trial was conducted in accordance with the International Conference on Harmonisation (ICH), Good Clinical Practices (GCP), Good Manufacturing Practice (GMP), the ethical principles of the Declaration of Helsinki and with applicable local regulations. This trial was conducted by qualified persons who respected the rights and welfare of the subjects and after the review and approval of the protocol by an EC. Adverse events were collected during the trial and subject was followed by 4 days after the trial.

Background therapy:

The investigational medicinal product (IMP) in this study is ESL as an oral suspension of 50 mg/mL with 3 different flavours to be tasted but not swallowed. Each of the 3 samples of IMP will consist of 2.5 mL and are to be administered using a spoon. The child is to swill the sample in their mouth for 15-30 seconds before spitting the sample out.

Evidence for comparator: -

Actual start date of recruitment	14 December 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	Romania: 23
Country: Number of subjects enrolled	Slovakia: 15
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	38
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:

Planned duration of study (from first subject first visit to last subject last visit): 3 months, with a recruitment period of about 2-3 months. Location of the trial is medical clinic.

Pre-assignment

Screening details:

Subjects who met all the inclusion criteria and none of the exclusion criteria were included in the clinical trial.

Pre-assignment period milestones

Number of subjects started	38
Number of subjects completed	38

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, Carer, Assessor

Blinding implementation details:

ESL will be provided in adequate container closure systems. Each container closure system label will bear at least the following information: name, address and phone number of sponsor, name of Principal Investigator, protocol code, randomisation number, packaging number, expiry date, storage conditions, pharmaceutical dosage form, route of administration, dosing instructions, and the following statements: “For clinical trial use only” and “Keep out of the sight and reach of children”.

Arms

Are arms mutually exclusive?	No
Arm title	ESL Banana taste

Arm description:

Eslicarbazepine acetate (ESL) Banana taste oral suspension with Banana flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2-093
Other name	Eslicarbazepine acetate (ESL)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the Study Day, all children will be given 3 different flavoured samples of ESL oral suspension for tasting, in the sequence to which they were randomised, in a double-blind, standardized setting. Each sample will consist of 2.5 mL and is to be given with a spoon in a double-blind manner, and is not to be swallowed. Hence, there should not be any treatment with ESL in this study. Should a subject swallow any of the 3 samples, no further samples are to be given, and appropriate follow-up measures will be taken

Arm title	ESL Grape taste

Arm description:

Eslicarbazepine acetate (ESL) Grape taste oral suspension with Grape flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses

Arm type	Experimental

Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2-093
Other name	Eslicarbazepine acetate (ESL)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the Study Day, all children will be given 3 different flavoured samples of ESL oral suspension for tasting, in the sequence to which they were randomised, in a double-blind, standardized setting. Each sample will consist of 2.5 mL and is to be given with a spoon in a double-blind manner, and is not to be swallowed. Hence, there should not be any treatment with ESL in this study. Should a subject swallow any of the 3 samples, no further samples are to be given, and appropriate follow-up measures will be taken

Arm title	ESL Tutti-Frutti taste

Arm description:

Eslicarbazepine acetate (ESL) Tutti-Frutti taste oral suspension with Tutti-Frutti flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2-093
Other name	Eslicarbazepine acetate (ESL)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the Study Day, all children will be given 3 different flavoured samples of ESL oral suspension for tasting, in the sequence to which they were randomised, in a double-blind, standardized setting. Each sample will consist of 2.5 mL and is to be given with a spoon in a double-blind manner, and is not to be swallowed. Hence, there should not be any treatment with ESL in this study. Should a subject swallow any of the 3 samples, no further samples are to be given, and appropriate follow-up measures will be taken

Number of subjects in period 1	ESL Banana taste	ESL Grape taste	ESL Tutti-Frutti taste
Started	38	38	38
Completed	38	38	38

Baseline characteristics

Reporting groups	
Reporting group title	ESL Banana taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Banana taste oral suspension with Banana flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	
Reporting group title	ESL Grape taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Grape taste oral suspension with Grape flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	
Reporting group title	ESL Tutti-Frutti taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Tutti-Frutti taste oral suspension with Tutti-Frutti flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	

Reporting group values	ESL Banana taste	ESL Grape taste	ESL Tutti-Frutti taste
Number of subjects	38	38	38
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	38	38	38
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	0	0	0
From 65 – 84 years	0	0	0
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	6.1	6.1	6.1
standard deviation	± 0.8	± 0.8	± 0.8
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	17	17	17
Male	21	21	21

Reporting group values	Total		
Number of subjects	38		
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0		
Preterm newborn- gestational age < 37 wk	0		

Newborns (0-27days)	0		
Infants and toddlers (28days – 23months)	0		
Children (2-11 years)	38		
Adolescents (12-17 year)	0		
From 18 - 64 years	0		
From 65 – 84 years	0		
Over 85 years	0		
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	17		
Male	21		

End points

End points reporting groups

Reporting group title	ESL Banana taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Banana taste oral suspension with Banana flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	
Reporting group title	ESL Grape taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Grape taste oral suspension with Grape flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	
Reporting group title	ESL Tutti-Frutti taste
Reporting group description:	
Eslicarbazepine acetate (ESL) Tutti-Frutti taste oral suspension with Tutti-Frutti flavour at a concentration of 50 mg/mL and was administered in 2.5 mL doses	
Subject analysis set title	Eslicarbazepine Acetate
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects who received at least 1 sample of IMP and made at least 1 taste assessment	

Primary: Overall taste assessment using Visual Analogue Scale (VAS)

End point title	Overall taste assessment using Visual Analogue Scale (VAS)[1]
End point description:	
Subject preference of 3 flavours of the ESL oral suspension assessed using 10 cm VAS.	
End point type	Primary
End point timeframe:	
1 day	

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: Statistical analysis for end point of overall taste assessment using Visual Analogue Scale (VAS) has not been provided as no confidence intervals were applicable. The overall taste assessment using Visual Analogue Scale (VAS) score was analyzed using a 1-way analysis of variance for repeated measures with the Tukey multiple comparison procedure: Least square mean=21.8, standard error=11. 82, p-value=0.1633.

End point values	ESL Banana taste	ESL Grape taste	ESL Tutti-Frutti taste	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	38	38	
Units: Visual Analogue Scale (VAS)				
arithmetic mean (standard error)				
Visual Analogue Scale (VAS)	5.8 (± 3.5)	5.8 (± 3.5)	7.1 (± 3.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Overall taste best/worst assessment

End point title	Overall taste best/worst assessment[2]

End point description:

The subject’s assessment of the overall taste (best, worst)

End point type	Primary

End point timeframe:

1 day

Notes:

[2] - 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: Statistical analysis for end point of overall taste best/worse assessment has not been provided as no confidence intervals were applicable. A Chi-square test was performed on the preference data to test for uniform distribution of scores: p-value=0.1267.

End point values	ESL Banana taste	ESL Grape taste	ESL Tutti-Frutti taste	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	38	38	
Units: Percentage of Subjects				
number (confidence interval)				
Best: Percentage (CI)	29 (15 to 43)	32 (17 to 46)	40 (24 to 55)	
Worst: Percentage (CI)	37 (22 to 52)	45 (29 to 61)	18 (6 to 31)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

5 days

Adverse event reporting additional description:

After the first tasting of study treatment until 1-4 days after tasting the IMP

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Eslicarbazepine Acetate

Reporting group description:

All treated subjects

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: None of non-serious adverse events were reported during the trial.

Serious adverse events	Eslicarbazepine Acetate		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Laryngitis			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Eslicarbazepine Acetate		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 38 (0.00%)		

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

None reported