Clinical trial results:
A 24 weeks prospective open label multicenter study to evaluate the effect on seizure frequency, safety and tolerability of Trileptal® (oxcarbazepine) monotherapy in children with partial seizures

Summary

EudraCT number	2015-004465-87
Trial protocol	Outside EU/EEA
Global end of trial date	28 September 2007

Results information

Result version number	v1 (current)
This version publication date	31 December 2016
First version publication date	31 December 2016

Trial information

Trial identification

Sponsor protocol code	CTRI476BRU02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00275912
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH 4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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?	Yes
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	28 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 September 2007
Global end of trial reached?	Yes
Global end of trial date	28 September 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A 24 weeks prospective open label multicenter study to evaluate the effect on seizure frequency, safety and tolerability of Trileptal® (oxcarbazepine) monotherapy in children with partial seizures

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 September 2006
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	Russian Federation: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

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)	2
Children (2-11 years)	8
Adolescents (12-17 years)	50
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:

A total of 60 subjects were enrolled in the study.

Period 1

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

Blinding implementation details:

open label

Arms

Arm title	Trileptal

Arm description:

Trileptal daily doses received by 58 patients varied from 240 up 1800 mg daily

Arm type	Experimental
Investigational medicinal product name	oxcarbazepine
Investigational medicinal product code	TRI476
Other name	Trileptal
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In the 1st day, 200 mg of carbamazepine (1/2 tablet) was replaced by 300 mg of Trileptal® (1 tablet). Further each 2-3 days 200 mg of carbamazepine was replaced with 300 mg of Trileptal® until conversion to the monotherapy. Single-time conversion was made in the following way: patient was given carbamazepine dose, then, the next day Trileptal® dose calculated from the dose ratio 1:1.5. The method of conversion was chosen by investigator depending on the patient's clinical state.

Number of subjects in period 1	Trileptal
Started	60
Completed	53
Not completed	7
Consent withdrawn by subject	1
Adverse event, non-fatal	4
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	60	60	
Age categorical			
Age Breakdown for children is not exactly known. 60 patients were between the ages of 7 months and 17 years. We know for that 8 patients at 2 sites are in the 2-11 age group and that 2 patients at 2 sites are in the infants and toddlers group (28 days to 23 months). The rest of the total distribution is unknown so the other 50 patients are dispersed among the 28 days to 17 years group.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Children age 6 mos to 17 years	60	60	
Age continuous			
Units: years			
arithmetic mean	9.46		
standard deviation	± 5.1	-	
Gender categorical			
Units: Subjects			
Female	29	29	
Male	31	31	

End points

End points reporting groups

Reporting group title	Trileptal
Reporting group description:	
Trileptal daily doses received by 58 patients varied from 240 up 1800 mg daily	

Primary: Rate of response (level of response at least 30% seizure frequency reduction compared to baseline)

End point title	Rate of response (level of response at least 30% seizure frequency reduction compared to baseline)[1]
End point description:	
Rate of seizures per week	
End point type	Primary
End point timeframe:	
week 1-24	

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: Summary results for only one arm...no comparison between groups

End point values	Trileptal			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Seizures				
arithmetic mean (standard deviation)				
Week 1	10.6 (± 41.86)			
Week 2	8 (± 30.25)			
Week 3	8.24 (± 33.45)			
Week 4	3.1 (± 10.54)			
Week 5	2 (± 5.59)			
Week 6	1.81 (± 6.86)			
Week 7	3.6 (± 18.44)			
Week 8	3.2 (± 18.44)			
Week 9	0.6 (± 1.93)			
Week 10	0.38 (± 1.38)			
Week 11	0.33 (± 1.31)			
Week 12	0.35 (± 1.46)			
Week 13	0.26 (± 1.76)			
Week 14	0.44 (± 2.46)			
Week 15	0.67 (± 4.45)			
Week 16	1.1 (± 7.16)			
Week 17	1.43 (± 9.93)			
Week 18	1.46 (± 9.53)			
Week 19	0.04 (± 0.19)			
Week 20	0.09 (± 0.35)			
Week 21	0.17 (± 0.64)			
Week 22	0.09 (± 0.49)			
Week 23	0.09 (± 0.45)			

Week 24	0.08 (± 0.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent responders week 7

End point title	Percent responders week 7

End point description:

The patients in whom seizure frequency has not decreased or has increased compared to baseline

End point type	Secondary

End point timeframe:

7 weeks

End point values	Trileptal			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percent				
number (confidence interval 95%)	90 (79 to 94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of "non-responders"

End point title	Percentage of "non-responders"

End point description:

percentage of "non-responders" (the patients in whom seizure frequency has not decreased or has increased compared to baseline);

End point type	Secondary

End point timeframe:

24 weeeks

End point values	Trileptal			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent				
number (not applicable)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: • percentage change in seizure frequency from baseline in all patients;

End point title	• percentage change in seizure frequency from baseline in all patients;
End point description: % reduction in Seizures	
End point type	Secondary
End point timeframe: 24 weeks	

End point values	Trileptal			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Pecent Change				
number (not applicable)	-98.1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until LSLV.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	oxcarbazepine

Reporting group description: -

Serious adverse events	oxcarbazepine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	oxcarbazepine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 60 (38.33%)		
Investigations			
AST rise			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
White cells rise			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
AP rise			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Eosinophils rise			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hb reduction			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Platelets reduction			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Serum Na reduction			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Vascular disorders			
Conduction abnormalities (ECG)			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Nervous system disorders			
Craniocerebral trauma			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Ataxia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Slow response			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Weakness of extremities			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Serial seizures			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Sleepiness			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	9		
Tremor of hands			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Astenia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Eye disorders			
Redness of conjunctiva			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Swelling of eyelid			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Itching			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Edema			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		

Infections and infestations Respiratory tract infection subjects affected / exposed occurrences (all) Varicella subjects affected / exposed occurrences (all)	 7 / 60 (11.67%) 9 1 / 60 (1.67%) 1		
Metabolism and nutrition disorders Body weight rise subjects affected / exposed occurrences (all) Appetite rise subjects affected / exposed occurrences (all)	 2 / 60 (3.33%) 2 1 / 60 (1.67%) 1		

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