Clinical trial results:
A 52 weeks, open-label, multicenter study evaluating the efficacy and safety of gabapentin as adjunctive therapy in pediatric subjects who have completed the 12 weeks treatment in study A9451162.

Summary

EudraCT number	2014-004175-23
Trial protocol	Outside EU/EEA
Global end of trial date	22 December 2010

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	A9451165

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00620555
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.govCallCenter@pfizer.com
Scientific contact	Pfizer Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.govCallCenter@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 February 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of gabapentin in the 52 weeks as add-on therapy in the treatment of pediatric subjects with partial seizures (including secondarily generalized) when other antiepileptics do not provide satisfactory effects.

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	28 May 2008
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	Japan: 65
Worldwide total number of subjects	65
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)	0
Children (2-11 years)	47
Adolescents (12-17 years)	18
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:

The study was initiated on 28 May 2008 and completed on 22 Dec 2010. A total of 65 subjects were enrolled in the study.

Period 1

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

Arms

Arm title	Gabapentin

Arm description:

Pediatric subjects received gabapentin three times daily for 52 weeks. Subjects aged 3 to 12 years received oral solution based on their body weight and subjects aged 13 to 15 years received gabapentin tablets. The dose was adjusted within the range of maintenance doses.

Arm type	Experimental
Investigational medicinal product name	Gabapentin
Investigational medicinal product code	CI-945
Other name	
Pharmaceutical forms	Oral solution, Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects aged 3 to 12 years received oral solution (250 milligram(mg)/5 milliliter(mL)) at the dose calculated based on their body weight; 40 milligram/kilogram/day (mg/kg/day) for 3 to 4 years old and 25 to 35 mg/kg/day for 5 to 12 years old but not exceeding 1800 milligram(mg) per day. Subjects aged 13 to 15 years received gabapentin tablet at the dose of 1200 or 1800 mg/day. The dose was adjusted within the range of maintenance doses. Gabapentin could be increased if necessary with the maximum dose of 50 mg/kg/day for subjects aged 3 to 12 years. All subjects could receive gabapentin tablet not exceeding 2400 mg per day.

Number of subjects in period 1	Gabapentin
Started	65
Completed	44
Not completed	21
Consent withdrawn by subject	1
Choice of other treatment	1
Adverse event, non-fatal	4
Protocol violation	2
Lack of efficacy	12
Visit failure against planned	1

Baseline characteristics

Reporting groups	
Reporting group title	Gabapentin
Reporting group description:	
Pediatric subjects received gabapentin three times daily for 52 weeks. Subjects aged 3 to 12 years received oral solution based on their body weight and subjects aged 13 to 15 years received gabapentin tablets. The dose was adjusted within the range of maintenance doses.	

Reporting group values	Gabapentin	Total	
Number of subjects	65	65	
Age categorical Units: Subjects			
3-4 years	8	8	
5-12 years	42	42	
13-16 years	15	15	
Gender categorical Units: Subjects			
Female	27	27	
Male	38	38	

End points

End points reporting groups

Reporting group title	Gabapentin

Reporting group description:

Pediatric subjects received gabapentin three times daily for 52 weeks. Subjects aged 3 to 12 years received oral solution based on their body weight and subjects aged 13 to 15 years received gabapentin tablets. The dose was adjusted within the range of maintenance doses.

Primary: Number of Subjects With Treatment-Emergent Adverse Events (All Causalities and Treatment-Related)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (All Causalities and Treatment-Related)[1]

End point description:

Any untoward medical occurrence in a subject who received study drug was considered an adverse event (AE), without regard to possibility of causal relationship. Treatment-emergent adverse events: those which occurred or worsened after baseline. Severe AEs: those which interferes significantly with subject's usual function. An AE resulting in any of the following outcomes, was considered to be a serious adverse event: death; life-threatening; initial or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect. Safety analysis set: All subjects who have received at least one dose of the study drug.

End point type	Primary

End point timeframe:

Up to 53 weeks

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: No statistical test was planned to be reported for this endpoint.

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Subjects				
number (not applicable)				
All-causality adverse events (AEs)	58			
Treatment-related AEs	13			
All-causality serious AEs	2			
Treatment-related serious AEs	0			
All-causality severe AEs	1			
Treatment-related severe AEs	0			
Discontinuation due to all-causality AEs	4			
Discontinuation due to treatment-related AEs	2			
Dose reduction due to all-causality AE	2			
Dose reduction due to treatment-related AEs	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Response Ratio

End point title	Response Ratio

End point description:

The Response Ratio calculated by the following equation : Response Ratio = (T minus B) divided by (T plus B), where T is seizure frequency per 28 days (i.e., the number of seizures per 28 days) calculated from the total number of seizures for the 52-week treatment period, and B is seizure frequency per 28 days (i.e., the number of seizures per 28 days) calculated from the total number of seizures for the 6-week baseline period of the previous study A9451162 (NCT00603473). Intent to treat (ITT): Subjects who have received at least one dose of the study drug and in whom the number of epileptic seizures used for efficacy assessment has been counted in both the baseline and treatment periods. n=number of subjects who have total number of seizures at each assessment time point.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Ratio				
arithmetic mean (standard deviation)				
Week 1 to 8 (n=65)	-0.263 (± 0.3141)			
Week 9 to 16 (n=60)	-0.256 (± 0.3513)			
Week 17 to 24 (n=58)	-0.3 (± 0.3671)			
Week 25 to 36 (n=54)	-0.28 (± 0.3753)			
Week 37 to 52 (n=47)	-0.327 (± 0.3712)			

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Rate

End point title	Responder Rate

End point description:

Responder Rate was defined as the percentage of subjects with a 50 percent or greater reduction in the seizure frequency per 28 days for the 52-week treatment period in comparison with the frequency per 28 days for the 6-week baseline period of the previous study A9451162 (NCT00603473). Intent to treat (ITT): Subjects who have received at least one dose of the study drug and in whom the number of epileptic seizures used for efficacy assessment has been counted in both the baseline and treatment periods. n=number of subjects who have total number of seizures at each assessment time point.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage of subjects				
number (confidence interval 95%)				
Week 1 to 8 (n=65)	35.4 (23.9 to 48.2)			
Week 9 to 16 (n=60)	40 (27.6 to 53.5)			
Week 17 to 24 (n=58)	39.7 (27.1 to 53.4)			
Week 25 to 36 (n=54)	40.7 (27.6 to 55)			
Week 37 to 52 (n=47)	46.8 (32.1 to 61.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Seizure Frequency

End point title	Percent Change in Seizure Frequency

End point description:

Percent change in seizure frequency (PCH) was calculated as follows: PCH = 100*(T minus B) divided by B, where T is seizure frequency per 28 days (i.e., the number of seizures per 28 days) calculated from the total number of seizures for the 52-week treatment period, and B is
seizure frequency per 28 days (i.e., the number of seizures per 28 days) calculated from the total number of seizures for the 6-week baseline period of the previous study A9451162 (NCT00603473).
Intent to treat (ITT): Subjects who have received at least one dose of the study drug and in whom the number of epileptic seizures used for efficacy assessment has been counted in both the baseline and treatment periods. n=number of subjects who have total number of seizures at each assessment time point.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percent change				
median (full range (min-max))				
Week 1 to 8 (n=65)	-34.2 (-100 to 63.1)			

Week 9 to 16 (n=60)	33 (-100 to 99.8)			
Week 17 to 24 (n=58)	-42 (-100 to 112.5)			
Week 25 to 36 (n=54)	-41.6 (-100 to 110.7)			
Week 37 to 52 (n=47)	-49.2 (-100 to 131.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 weeks

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study. EU BR specific AE tables were generated using latest coding.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	GABAPENTIN

Reporting group description:

Pediatric subjects received gabapentin three times daily for 52 weeks. Subjects aged 3 to 12 years received oral solution based on their body weight and subjects aged 13 to 15 years received gabapentin tablets. The dose was adjusted within the range of maintenance doses.

Serious adverse events	GABAPENTIN		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 65 (3.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Encephalopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	GABAPENTIN		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 65 (73.85%)		
Injury, poisoning and procedural complications			
Arthropod bite			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	5		
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	9		
Nervous system disorders			
Somnolence			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 65 (15.38%)		
occurrences (all)	11		
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 65 (12.31%)		
occurrences (all)	28		
Gastrointestinal disorders			
Dental caries			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 65 (7.69%)		
occurrences (all)	6		
Diarrhoea			
alternative assessment type: Non-systematic			

subjects affected / exposed	7 / 65 (10.77%)		
occurrences (all)	10		
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Eczema			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	8		
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 65 (13.85%)		
occurrences (all)	9		
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	28 / 65 (43.08%)		
occurrences (all)	52		
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	10		
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 65 (6.15%)		
occurrences (all)	12		

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