Clinical trial results:
An Open-Label, Multicenter Study Evaluating, The Efficacy, Safety And Pharmacokinetics Of Gabapentin As Adjunctive Therapy In Pediatric Subjects With Partial Seizures When Other Antiepileptics Do Not Provide Satisfactory Effects

Summary

EudraCT number	2014-004174-42
Trial protocol	Outside EU/EEA
Global end of trial date	24 December 2009

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	A9451162

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00603473
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	Clinical Trials.gov Call Center, Pfizer Inc, 1 8007181021, ClinicalTrials.govCallCenter@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc, 1 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 April 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 December 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study was intended to evaluate the efficacy, safety and pharmacokinetics of gabapentin administered for 12 weeks as adjunctive therapy in pediatric epilepsy subjects with partial seizures (including secondary generalized seizures) with no satisfactory response to other antiepileptics.

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	10 January 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: 89
Worldwide total number of subjects	89
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)	67
Adolescents (12-17 years)	22
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened at 27 centers in Japan.

Pre-assignment

Screening details:

90 subjects were enrolled in the study. Of them, 89 received the study treatment, while 1 withdrew consent.

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:

The dosage of oral solution for subjects aged 3 to 12 years was calculated based on their body weight. The dose was titrated for the first 3 days of the treatment period. Doses were administered as per subject's age ranges (ranging between 3 to 4 years, 5 to 12 years, and 13 to 15 years) on Day 1 up to 3. After Day 3, the dose was adjusted if necessary within the range of maintenance doses.

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

Dosage and administration details:

The dosage of oral solution for subjects aged 3 to 12 years was calculated based on their body weight. The dose was titrated for the first 3 days of the treatment period. Subjects aged 3 to 4 years received gabapentin 10 milligram per kilogram per day (mg/kg/day) on Day 1, 20 mg/kg/day on Day 2 and 40 mg/kg/day from Day 3. Subjects aged 5 to 12 years received gabapentin 10 mg/kg/day on Day 1, 20 mg/kg/day on Day 2 and 25 to 35 mg/kg/day from Day 3. Subjects aged 13 to 15 years received gabapentin 600 mg/day on Day 1, 1200 mg/day on Day 2 and 1200 or 1800 mg/day from Day 3. After Day 3, the dose was adjusted if necessary within the range of maintenance doses. The maximum daily dose was 600 mg for Day 1, 1200 mg for Day 2, and 1800 mg for Day 3 and thereafter.

Number of subjects in period 1	Gabapentin
Started	89
Completed	80
Not completed	9
Adverse event, non-fatal	4
Protocol violation	1
Lack of efficacy	4

Baseline characteristics

Reporting groups	
Reporting group title	Gabapentin
Reporting group description:	
The dosage of oral solution for subjects aged 3 to 12 years was calculated based on their body weight. The dose was titrated for the first 3 days of the treatment period. Doses were administered as per subject's age ranges (ranging between 3 to 4 years, 5 to 12 years, and 13 to 15 years) on Day 1 up to 3. After Day 3, the dose was adjusted if necessary within the range of maintenance doses.	

Reporting group values	Gabapentin	Total	
Number of subjects	89	89	
Age categorical Units: Subjects			
3-4 years	11	11	
5-12 years	63	63	
13-15 years	15	15	
Gender categorical Units: Subjects			
Female	40	40	
Male	49	49	

End points

End points reporting groups

Reporting group title	Gabapentin

Reporting group description:

The dosage of oral solution for subjects aged 3 to 12 years was calculated based on their body weight. The dose was titrated for the first 3 days of the treatment period. Doses were administered as per subject's age ranges (ranging between 3 to 4 years, 5 to 12 years, and 13 to 15 years) on Day 1 up to 3. After Day 3, the dose was adjusted if necessary within the range of maintenance doses.

Primary: Response Ratio of Gabapentin in Japanese Pediatric Subjects with Partial Seizures

End point title	Response Ratio of Gabapentin in Japanese Pediatric Subjects with Partial Seizures[1]

End point description:

The Response Ratio calculated by the following equation was assessed as the primary endpoint: R Ratio = (T−B) / (T+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 12-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. Modified intent-to-treat (MITT) population: Subjects who have received the study medication for at least 28 days and in whom the number of epileptic seizures used for efficacy assessment has been counted for at least 28 days in both the baseline and treatment periods.

End point type	Primary

End point timeframe:

12 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: Only descriptive data was planned to be reported.

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: Ratio				
arithmetic mean (confidence interval 95%)	-0.158 (-0.221 to -0.096)			

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 12-week treatment period in comparison with the frequency per 28 days for the 6-week baseline period. Modified intent-to-treat (MITT) population: Subjects who have received the study medication for at least 28 days and in whom the number of epileptic seizures used for efficacy assessment has been counted for at least 28 days in both the baseline and treatment

periods.

End point type	Secondary

End point timeframe:

12 Weeks

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: Percentage of subjects				
arithmetic mean (confidence interval 95%)	19.8 (12 to 29.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Seizure Frequency (PCH)

End point title	Percent Change in Seizure Frequency (PCH)

End point description:

PCH calculated by the following equation was assessed as secondary endpoint. PCH = 100 (T−B) / 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 12-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. Modified intent-to-treat (MITT) population: Subjects who have received the study medication for at least 28 days and in whom the number of epileptic seizures used for efficacy assessment has been counted for at least 28 days in both the baseline and treatment periods.

End point type	Secondary

End point timeframe:

12 Weeks

End point values	Gabapentin			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: Percent change				
median (full range (min-max))	-24.4 (-100 to 192.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12-week treatment period, 1-week follow-up period

Adverse event reporting additional description:

The same event may appear as both an AE and 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 separately using latest coding.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	GABAPENTIN

Reporting group description:

The dosage of oral solution for subjects aged 3 to 12 years was calculated based on their body weight. The dose was titrated for the first 3 days of the treatment period. Doses were administered as per subject's age ranges (ranging between 3 to 4 years, 5 to 12 years, and 13 to 15 years) on Day 1 up to 3. After Day 3, the dose was adjusted if necessary within the range of maintenance doses.

Serious adverse events	GABAPENTIN		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 89 (1.12%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	GABAPENTIN		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 89 (82.02%)		
Injury, poisoning and procedural complications			

Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 89 (6.74%)		
occurrences (all)	7		
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 89 (7.87%)		
occurrences (all)	10		
Nervous system disorders			
Ataxia			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Somnolence			
alternative assessment type: Non-systematic			
subjects affected / exposed	35 / 89 (39.33%)		
occurrences (all)	39		
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 89 (5.62%)		
occurrences (all)	8		
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 89 (6.74%)		
occurrences (all)	6		
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		

Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 89 (5.62%)		
occurrences (all)	5		
Infections and infestations			
Conjunctivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 89 (10.11%)		
occurrences (all)	9		
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	24 / 89 (26.97%)		
occurrences (all)	32		
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 89 (6.74%)		
occurrences (all)	9		
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	4		
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 89 (4.49%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		

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