



## 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:

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**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:

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**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:

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**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:

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**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<br>Units: Subjects    |            |       |  |
| 3-4 years                             | 11         | 11    |  |
| 5-12 years                            | 63         | 63    |  |
| 13-15 years                           | 15         | 15    |  |
| Gender categorical<br>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 <sup>[1]</sup> |
|-----------------|--|

End point description:

The Response Ratio calculated by the following equation was assessed as the primary endpoint:  $R \text{ Ratio} = (T-B) / (T+B)$  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             |           |

|   |                   |  |  |  |
|---|-------------------|--|--|--|
| <b>End point values</b>                   | 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:   |   |
| <p>PCH calculated by the following equation was assessed as secondary endpoint. <math>PCH = 100 (T - B) / B</math> 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.</p> |   |
| End point type   | Secondary                                 |
| End point timeframe:   |   |
| 12 Weeks   |   |

|                               |                       |  |  |  |
|-------------------------------|-----------------------|--|--|--|
| <b>End point values</b>       | 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        |                  |  |  |



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

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



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported