Clinical trial results:
A Placebo-Controlled, Double-Blind Comparative Study of E2080 in Lennox-Gastaut Syndrome Patients

Summary

EudraCT number	2016-004952-30
Trial protocol	Outside EU/EEA
Global end of trial date	12 August 2011

Results information

Result version number	v1 (current)
This version publication date	21 February 2018
First version publication date	21 February 2018

Trial information

Trial identification

Sponsor protocol code	E2080-J081-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01146951
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Co., Ltd.
Sponsor organisation address	4-6-10 Koishikawa, Bunkyo-ku, Tokyo, Japan, 112-8088
Public contact	Customer Joy Department. EJ, Eisai Co., Ltd., Eisai Co., Ltd., 81(03) 3817-3700,
Scientific contact	Customer Joy Department. EJ, Eisai Co., Ltd., Eisai Co., Ltd., 81(03) 3817-3700,

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 August 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate that the efficacy of E2080 in percent change in tonic-atonic seizure frequency in participants with Lennox-Gastaut Syndrome (LGS) relative to placebo.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following:
- Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008)
- International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
- Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312
- European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states.
- Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2010
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: 58
Worldwide total number of subjects	58
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)	23
Adolescents (12-17 years)	13
Adults (18-64 years)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of n= 66 who started Observation Period, 7 discontinued from study. Primary reasons were deviation of the inclusion/ exclusion criteria (n=5), untoward event before study treatment (n=1) & other (n=1). Of 59 participants, 58 were included in Full Analysis Set. 1 participant (E2080 group) was excluded due to inappropriate diagnosis of disease.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Rufinamide (E2080)

Arm description:

Rufinamide : Rufinamide tablets administered orally twice daily after breakfast and dinner. Treatment was divided into a Dose Titration Period (2 weeks) and a Dose Maintenance Period (10 weeks). As a general rule, the dose was increased by 1 step every 2 days until it reached the target maintenance dose determined by body weight at the start of the Observation Period.
Target maintenance dose:
15.0 - 30.0 kilograms (kg): 1000 milligrams/day (mg/day) (5 tablets each in the morning and evening)
30.1 - 50.0 kg: 1800 mg/day (4 tablets in the morning and 5 in the evening)
50.1 - 70.0 kg: 2400 mg/day (6 tablets each in the morning and evening)
>= 70.1 kg: 3200 mg/day (8 tablets each in the morning and evening)

Arm type	Experimental
Investigational medicinal product name	Rufinamide
Investigational medicinal product code	E2080
Other name	Banzel
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rufinamide tablets administered orally twice daily after breakfast and dinner. Treatment was divided into a Dose Titration Period (2 weeks) and a Dose Maintenance Period (10 weeks). As a general rule, the dose was increased by 1 step every 2 days until it reached the target maintenance dose determined by body weight at the start of the Observation Period.
Target maintenance dose:
15.0 - 30.0 kg: 1000 mg/day (5 tablets each in the morning and evening)
30.1 - 50.0 kg: 1800 mg/day (4 tablets in the morning and 5 in the evening)
50.1 - 70.0 kg: 2400 mg/day (6 tablets each in the morning and evening)
>= 70.1 kg: 3200 mg/day (8 tablets each in the morning and evening)

Arm title	Placebo

Arm description:

Placebo : Rufinamide Matching Placebo tablets administered orally twice daily after breakfast and dinner for a total of 12 weeks

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rufinamide Matching Placebo tablets administered orally twice daily after breakfast and dinner for a total of 12 weeks.

Number of subjects in period 1	Rufinamide (E2080)	Placebo
Started	28	30
Completed	24	29
Not completed	4	1
Adverse event, non-fatal	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Rufinamide (E2080)
Reporting group description:	
Rufinamide : Rufinamide tablets administered orally twice daily after breakfast and dinner. Treatment was divided into a Dose Titration Period (2 weeks) and a Dose Maintenance Period (10 weeks). As a general rule, the dose was increased by 1 step every 2 days until it reached the target maintenance dose determined by body weight at the start of the Observation Period. Target maintenance dose: 15.0 - 30.0 kilograms (kg): 1000 milligrams/day (mg/day) (5 tablets each in the morning and evening) 30.1 - 50.0 kg: 1800 mg/day (4 tablets in the morning and 5 in the evening) 50.1 - 70.0 kg: 2400 mg/day (6 tablets each in the morning and evening) >= 70.1 kg: 3200 mg/day (8 tablets each in the morning and evening)	
Reporting group title	Placebo
Reporting group description:	
Placebo : Rufinamide Matching Placebo tablets administered orally twice daily after breakfast and dinner for a total of 12 weeks	

Reporting group values	Rufinamide (E2080)	Placebo	Total
Number of subjects	28	30	58
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	10	13	23
Adolescents (12-17 years)	6	7	13
Adults (18-64 years)	12	10	22
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
One participant from the Rufinamide (E2080) group was excluded from the Full Analysis Set because of the inappropriate diagnosis of the disease, dropping the total number from 29 to 28 participants.			
Units: years			
arithmetic mean	16	13.9	
standard deviation	± 7.1	± 6.1	-
Gender categorical			
One subject from the Rufinamide (E2080) group was excluded from the FAS because of the inappropriate diagnosis of the disease, dropping the total number from 29 to 28 participants.			
Units: Subjects			
Female	11	11	22
Male	17	19	36

End points

End points reporting groups

Reporting group title	Rufinamide (E2080)

Reporting group description:

Rufinamide : Rufinamide tablets administered orally twice daily after breakfast and dinner. Treatment was divided into a Dose Titration Period (2 weeks) and a Dose Maintenance Period (10 weeks). As a general rule, the dose was increased by 1 step every 2 days until it reached the target maintenance dose determined by body weight at the start of the Observation Period.
Target maintenance dose:
15.0 - 30.0 kilograms (kg): 1000 milligrams/day (mg/day) (5 tablets each in the morning and evening)
30.1 - 50.0 kg: 1800 mg/day (4 tablets in the morning and 5 in the evening)
50.1 - 70.0 kg: 2400 mg/day (6 tablets each in the morning and evening)
>= 70.1 kg: 3200 mg/day (8 tablets each in the morning and evening)

Reporting group title	Placebo

Reporting group description:

Placebo : Rufinamide Matching Placebo tablets administered orally twice daily after breakfast and dinner for a total of 12 weeks

Primary: Percent Change in Tonic-Atonic Seizure Frequency from Baseline (Per 28 days)

End point title	Percent Change in Tonic-Atonic Seizure Frequency from Baseline (Per 28 days)

End point description:

The sum of the frequencies of tonic seizures and atonic seizures was defined as the "tonic-atonic seizure frequency". The percent change in tonic-atonic seizure frequency per 28 days was assessed. The percent change in tonic-atonic seizure frequency was calculated using the tonic-atonic seizure frequency per 28 days of the Observation Period as the baseline and the tonic-atonic seizure frequency per 28 days of the Treatment Period as the post-treatment value. Percentage change in tonic-atonic seizure frequency was calculated as follows: [100 x (post-treatment value-baseline)/baseline]. The frequency of epileptic seizures was recorded in the seizure diary by the recorder. Seizure frequency was counted based on the classification established by the International League Against Epilepsy (ILAE). The diary recorder monitored the participant and recorded the seizure diary in a consistent manner, and continued these practices throughout the study period. Full Analysis Set (FAS) was analyzed.

End point type	Primary

End point timeframe:

Baseline (28 day observational period) and End of Treatment (28 day treatment period)

End point values	Rufinamide (E2080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: Percent Change				
median (full range (min-max))	-24.2 (-93.5 to 27.2)	-3.25 (-81.6 to 151.9)		

Statistical analyses

Statistical analysis title	Analysis of seizure frequecy
Comparison groups	Placebo v Rufinamide (E2080)
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges–Lehmann
Point estimate	-26.65
Confidence interval	
level	90 %
sides	2-sided
lower limit	-40.3
upper limit	-11.8

Secondary: Number of Participants achieving a 50% reduction in tonic-atonic	
End point title	Number of Participants achieving a 50% reduction in tonic-atonic
End point description:	
50% Responder Rate in Tonic-Atonic Seizure Frequency was presented as the number of participants who achieved a 50% reduction in tonic-atonic seizure frequency. FAS was defined as participants who were registered for the Treatment Period and excludes those listed below; Participants who did not meet the inclusion criterion related the target disease, participants who did not take the study drug, participants without any evaluable efficacy data after the start of study treatment.	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Rufinamide (E2080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: Participants				
number (not applicable)				
Yes (50% Reduction Achieved)	7	2		
No	21	28		

Statistical analyses

Statistical analysis title	Analysis of 50% reduction in seizures
Comparison groups	Placebo v Rufinamide (E2080)

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	Fisher exact

Secondary: Percent Change in Total Seizure Frequency (Per 28 days)

End point title	Percent Change in Total Seizure Frequency (Per 28 days)

End point description:

Percent change in the total seizure frequency (per 28 days) was calculated using the total seizure frequency per 28 days of the Observation Period as the baseline and the total seizure frequency per 28 days of the Treatment Period as the post-treatment value. Percentage change in total seizure frequency was calculated as follows: [100 x (post-treatment value - baseline)/ baseline]. Full analysis set (FAS) is defined as participants who were registered for the Treatment Period and excludes those listed below. Participants who did not meet the inclusion criterion related the target disease, participants who did not take the study drug, participants without any evaluable efficacy data after the start of study treatment.

End point type	Secondary

End point timeframe:

Baseline (28 day observational period) and End of Treatment (28 day treatment period)

End point values	Rufinamide (E2080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: Percent Change				
median (full range (min-max))	-32.9 (-87.3 to 15.4)	-3.05 (-52.2 to 133)		

Statistical analyses

Statistical analysis title	Analysis of total seizure frequency
Comparison groups	Rufinamide (E2080) v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-33.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-47.1
upper limit	-17

Secondary: Percentage change in the frequency of seizures other than tonic-atonic seizures (per 28 days)

End point title	Percentage change in the frequency of seizures other than tonic-atonic seizures (per 28 days)

End point description:

Percent change in the frequency of seizures other than tonic-atonic seizures (per 28 days) was calculated using the total seizure frequency per 28 days of the Observation Period as the baseline and the total seizure frequency per 28 days of the Treatment Period as the post-treatment value. Percentage change in total seizure frequency was calculated as follows: [100 x (post-treatment value - baseline)/ baseline]. Seizures analyzed other than tonic-atonic seizures included: Partial seizure freq. (frequency), Absence seizure, Atyp. (atypical) absence seizure, Myoclonic seizure, Clonic seizure, Tonic seizure, Tonic-clonic seizure, Atonic seizure, & Uncla. (unclassified) epileptic seizure. The frequency of epileptic seizures was recorded in the diary by the recorder. Seizure frequency was counted based on the classification established by the International League Against Epilepsy (ILAE). The diary recorder monitored the participant and recorded the seizure diary in a consistent manner.

End point type	Secondary

End point timeframe:

Baseline (28 day observational period) and End of Treatment (28 day treatment period)

End point values	Rufinamide (E2080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: Percent change				
median (full range (min-max))				
Partial Seizure Freq. % Change (n=4,6)	-52.2 (-96.2 to -26.3)	4.5 (-28.2 to 35.9)		
Absence Seizure Freq. % Change (n=1,0)	3.4 (3.4 to 3.4)	0 (0 to 0)		
Atyp. Absence Seizure Freq. % Change (n=12,19)	-59 (-100 to 107.1)	-21.1 (-83.2 to 253.5)		
Myoclonic Seizure Freq. % Change (n=10,10)	-52.35 (-100 to 53.3)	6.6 (-46.1 to 270)		
Clonic Seizure Freq. % Change (n=1,0)	-81.2 (-81.2 to -81.2)	0 (0 to 0)		
Tonic Seizure Freq. % Change (n=28,28)	-24.2 (-92.6 to 42.8)	-3.6 (-83.8 to 274.8)		
Tonic-clonic Seizure Freq. % Change (n=2,10)	-57.35 (-100 to -14.7)	2.35 (-75.8 to 450)		
Atonic Seizure Freq. % Change (n=10,12)	-63.1 (-100 to 68.8)	-6.1 (-100 to 2195.7)		
Uncla. Epileptic Seizure Freq. % Change (n=1,0)	-88.7 (-88.7 to -88.7)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Analysis for Partial Seizure Frequency
Comparison groups	Rufinamide (E2080) v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-57.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-104.5
upper limit	-17.3

Statistical analysis title	Analysis of atypical absence seizure frequency
Comparison groups	Placebo v Rufinamide (E2080)
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-28.65
Confidence interval	
level	90 %
sides	2-sided
lower limit	-72
upper limit	0.9

Statistical analysis title	Analysis for myoclonic seizure frequency
Comparison groups	Placebo v Rufinamide (E2080)
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-54.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-126.6
upper limit	-15.4

Statistical analysis title	Analysis of tonic seizure frequency

Comparison groups	Rufinamide (E2080) v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-23.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-40.7
upper limit	-5.6

Statistical analysis title	Analysis for Tonic-clonic seizure frequency
Comparison groups	Placebo v Rufinamide (E2080)
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.107
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-71.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-464.7
upper limit	30.5

Statistical analysis title	Analysis of Atonic seizure frequency
Comparison groups	Placebo v Rufinamide (E2080)
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges-Lehmann method
Point estimate	-52.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-89.1
upper limit	10.8

Secondary: Clinical Global Impression of Change (CGIC)

End point title	Clinical Global Impression of Change (CGIC)

End point description:

CGIC in participants with Lennox-Gastaut Syndrome relative to placebo was presented as number of participants in each category at the final assessment (last observation carried forward [LOCF]) & at Week 12 of the Treatment Period. The investigator assessed the CGIC by comparing the participants' condition during the 4 weeks immediately before the completion (or discontinuation [d/c]) of the Treatment Period to his/her condition during the 4-week Observation Period (for participants who d/c'd the study during the Treatment Period, the CGIC was assessed by comparing the participant's condition from the start to discontinuation of the study treatment to his/her condition during the 4-week Observation Period).
The CGIC was assessed according to the following 7-grade scale based on the frequency & severity of seizures, adverse events, and overall conditions of daily life.
Markedly improved, Improved, Slightly improved, Unchanged, Slightly worsened, Worsened, Markedly worsened.

End point type	Secondary

End point timeframe:

Up to Week 12 of the treatment period

End point values	Rufinamide (E2080)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	30		
Units: participants				
number (not applicable)				
Week 12: Markedly improved (n=25, 29)	0	0		
Week 12: Improved (n=25, 29)	9	0		
Week 12: Slightly Improved (n=25, 29)	4	9		
Week 12: Unchanged (n=25, 29)	10	18		
Week 12: Slightly Worsened (n=25, 29)	1	1		
Week 12: Worsened (n=25, 29)	1	1		
Week 12: Markedly Worsened (n=25, 29)	0	0		
LOCF: Markedly Improved (n=28, 30)	3	0		
LOCF: Improved (n=28, 30)	9	0		
LOCF: Slightly Improved (n=28, 30)	4	9		
LOCF: Unchanged (n=28, 30)	10	19		
LOCF: Slightly Worsened (n=28, 30)	1	1		
LOCF: Worsened (n=28, 30)	1	1		
LOCF: Markedly Worsened (n=28, 30)	0	0		

Statistical analyses

Statistical analysis title	Analysis of Week 12 of the Treatment Period
Comparison groups	Rufinamide (E2080) v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Analysis of final assessment (LOCF)
Comparison groups	Rufinamide (E2080) v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose until date of last dose of study treatment, up to approximately 1 year 2 months

Adverse event reporting additional description:

Treatment-emergent adverse events and treatment-emergent serious adverse events were reported for the safety analysis set, which consisted of participants who registered for the Treatment Period and excludes participants who did not take study drug and those without any evaluable safety data after the start of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Rufinamide (E2080)

Reporting group description:

Rufinamide tablets administered orally twice daily after breakfast and dinner. Treatment was divided into a Dose Titration Period (2 weeks) and a Dose Maintenance Period (10 weeks). As a general rule, the dose was increased by 1 step every 2 days until it reached the target maintenance dose determined by body weight at the start of the Observation Period. Target maintenance dose: 15.0 - 30.0 kg: 1000 mg/day (5 tablets each in the morning and evening) 30.1 - 50.0 kg: 1800 mg/day (4 tablets in the morning and 5 in the evening) 50.1 - 70.0 kg: 2400 mg/day (6 tablets each in the morning and evening) >= 70.1 kg: 3200 mg/day (8 tablets each in the morning and evening)

Reporting group title	Placebo

Reporting group description:

Rufinamide Matching Placebo tablets administered orally twice daily after breakfast and dinner for a total of 12 weeks.

Serious adverse events	Rufinamide (E2080)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rufinamide (E2080)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 29 (93.10%)	21 / 30 (70.00%)	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Stereotypy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood Pressure Decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood Pressure Increased			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	
occurrences (all)	1	2	

Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lymphocyte Count Decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Platelet Count Decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Excoriation			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Eye injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Subcutaneous Haematoma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tooth injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Autism			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Complex partial seizures			

subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Psychomotor Hyperactivity			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	6 / 29 (20.69%)	2 / 30 (6.67%)	
occurrences (all)	6	2	
Status Epilepticus			
subjects affected / exposed	8 / 29 (27.59%)	5 / 30 (16.67%)	
occurrences (all)	9	9	
Tonic Convulsion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Anal Fissure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Aphthous Stomatitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dental Caries			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Gingival Bleeding			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	5 / 29 (17.24%)	1 / 30 (3.33%)	
occurrences (all)	7	1	
Skin and subcutaneous tissue disorders			
Dry skin			

subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Purpura			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Skin chapped			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Heat rash			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hyperkeratosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Drug eruption			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Joint Swelling			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cellulitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastroenteritis			

subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	9 / 29 (31.03%)	9 / 30 (30.00%)	
occurrences (all)	10	9	
Otitis Media			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 29 (6.90%)	4 / 30 (13.33%)	
occurrences (all)	2	4	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	6 / 29 (20.69%)	2 / 30 (6.67%)	
occurrences (all)	6	2	
Dehydration			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2010	• Description of the method for examining concomitant drugs was modified. • Date and time of taking E2080 and concomitant AEDs immediately before blood sampling for plasma drug concentration measurements were deleted from the monitoring procedure. • Explanation to the investigator and sub investigator was added.
05 July 2010	• Check for blinding of the study drug before packaging the study drug by the allocation manager was deleted. • The study implementation structure of the sponsor and the responsible person were changed. • Matters to be described in the CRF (postponement of dose increase or reduction, and increase in the interval of tapering) were deleted from the identification of the source data.
13 October 2010	• Phenobarbital (suppository) was added to rescue drugs for status epilepticus. • The study implementation structure of the sponsor was changed. • Monitors were changed. • Responsible persons at the case registration center, emergency key code control center, and clinical research organization were changed.
11 April 2011	• The study implementation structure of the sponsor was changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported