Clinical trial results:
A Long Term Extension Study of E2080 in Patients with Lennox-Gastaut Syndrome

Summary

EudraCT number	2016-004953-34
Trial protocol	Outside EU/EEA
Global end of trial date	09 August 2013

Results information

Result version number	v1
This version publication date	15 March 2018
First version publication date	15 March 2018

Trial information

Trial identification

Sponsor protocol code	E2080-J081-305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01151540
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Medical Research Inc.
Sponsor organisation address	4-6-10 Koishikawa, Bunkyo-Ku, Tokyo, Japan,
Public contact	Customer Joy Department. EJ, Eisai Co., Ltd., 81 33817-3700,
Scientific contact	Customer Joy Department. EJ, Eisai Co., Ltd., 81 33817-3700,

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	25 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety of long term administration of E2080 in the participants with Lennox-Gastaut syndrome (LSG) who completed the E2080-J081-304 study.

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	19 November 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: 54
Worldwide total number of subjects	54
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)	22
Adolescents (12-17 years)	11
Adults (18-64 years)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who successfully completed Study 304 were enrolled into this study.

Period 1

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

Blinding implementation details:

Initially participants were blinded, then changed over to open-label for the remainder of the study as follows; 1) Pre-conversion Period - designed to avoid breaking the blindness in the preceding Study 304 and to prevent any data obtained in the open-label treatment in Study 305 from affecting the evaluation in the Study 304, and 2) Conversion Period - participants on placebo were titrated to the appropriate dose of rufinamide (the Study Drug B) within 2 weeks under double-blind conditions.

Arms

Arm title	Rufinamide

Arm description:

Ralfinamide was administered orally twice daily after breakfast and dinner. Participants on placebo in Study 304 were titrated over to rufinamide within 2 weeks during the Conversion Period. As a general rule, the dose of rufinamide at the end of the Conversion Period was maintained throughout the Maintenance Period.

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:

Ralfinamide was administered orally twice daily after breakfast and dinner.

Number of subjects in period 1	Rufinamide
Started	54
Completed	41
Not completed	13
Consent withdrawn by subject	7
Adverse event, non-fatal	4
Not specified	2

Baseline characteristics

Reporting groups	
Reporting group title	Rufinamide

Reporting group description:

Ralfinamide was administered orally twice daily after breakfast and dinner. Participants on placebo in Study 304 were titrated over to rufinamide within 2 weeks during the Conversion Period. As a general rule, the dose of rufinamide at the end of the Conversion Period was maintained throughout the Maintenance Period.

Reporting group values	Rufinamide	Total	
Number of subjects	54	54	
Age categorical Units: Subjects			
≥4 to <12 years	22	22	
≥12 to <17 years	11	11	
≥17 years	21	21	
Age continuous Units: years			
arithmetic mean	15.0		
standard deviation	± 6.8	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	33	33	

Subject analysis sets	
Subject analysis set title	Efficacy Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Efficacy Analysis Set included 46 participants. 8 participants who had no evaluable efficacy data were excluded.

Reporting group values	Efficacy Analysis Set		
Number of subjects	46		
Age categorical Units: Subjects			
≥4 to <12 years	18		
≥12 to <17 years	11		
≥17 years	17		
Age continuous Units: years			
arithmetic mean	15.2		
standard deviation	± 6.9		
Gender categorical Units: Subjects			
Female	16		
Male	30		

End points

End points reporting groups

Reporting group title	Rufinamide

Reporting group description:

Ralfinamide was administered orally twice daily after breakfast and dinner. Participants on placebo in Study 304 were titrated over to rufinamide within 2 weeks during the Conversion Period. As a general rule, the dose of rufinamide at the end of the Conversion Period was maintained throughout the Maintenance Period.

Subject analysis set title	Efficacy Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Efficacy Analysis Set included 46 participants. 8 participants who had no evaluable efficacy data were excluded.

Primary: Number of Participants with Adverse Events as a Measure of Safety and Tolerability of Rufinamide

End point title	Number of Participants with Adverse Events as a Measure of Safety and Tolerability of Rufinamide[1]

End point description:

Safety was assessed by monitoring and recording all adverse events (AEs), serious adverse events (SAEs), clinical laboratory tests, blood pressure, pulse rate, physical examination, and 12-lead electrocardiogram (ECG). Treatment-emergent adverse events (TEAEs) were defined as AEs that started on or after the date and time of administration of first dose of test drug, but not later than 30 days after discontinuation from the study, or if the AE was present prior to the administration of the first dose of test drug and increased in National Cancer Institute Common Toxicity Criteria (NCI CTC version 3.0) grade during the study or 30 days after discontinuation from the study. AEs were considered serious if it resulted in; death, was life-threatening, hospitalization/prolonged hospitalization, persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Safety analysis set included all treated participants.

End point type	Primary

End point timeframe:

From date of first dose up to 30 days after the last dose of study treatment, up to approximately 2 years 10 months

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: Statistical analysis was not performed on this data set.

End point values	Rufinamide			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: Participants				
number (not applicable)				
TEAEs	54			
Treatment-related TEAEs	38			
SAEs	9			
Treatment-related SAEs	2			
AEs leading to study drug withdrawal	3			
AEs leading to study drug dose reduction	12			

Statistical analyses

No statistical analyses for this end point

Secondary: 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 was calculated using the tonic-atonic seizure frequency per 28 days of the Observation Period in Study 304 as the baseline and the tonic-atonic seizure frequency at Weeks 12, 24, 32, 40, 52 and Week 52 Last Observation Carried Forward (LOCF) 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. The Efficacy Analysis Set was used.

End point type	Secondary

End point timeframe:

Baseline (Observation period in Study 304), Week 12, Week 24, Week 32, Week 40, Week 52 and Week 52 LOCF

End point values	Efficacy Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: Percent Change in Seizure Frequency				
median (full range (min-max))				
Baseline (n=46)	220.85 (8.3 to 22469.5)			
Percent Change in Week 12 (n=46)	-39.3 (-100 to 125.2)			
Percent Change in Week 24 (n=43)	-40.6 (-100 to 85.7)			
Percent Change in Week 32 (n=42)	-46.8 (-100 to 75)			
Percent Change in Week 40 (n=41)	-47.6 (-100 to 833.2)			
Percent Change in Week 52 (n=40)	-36.05 (-100 to 101.7)			
Percent Change in Week 52 LOCF (n=46)	-39.25 (-100 to 101.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in the Total Seizure Frequency From Baseline (Per 28 Days)

End point title	Percent Change in the Total Seizure Frequency From Baseline

	(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 of Study 304 as the baseline and the total seizure frequency per 28 days at Weeks 12, 24, 32, 40, 52 and Week 52 LOCF as the post-treatment value. Percentage change in total seizure frequency was calculated as follows: [100 x (post-treatment value - baseline)/ baseline].

End point type	Secondary

End point timeframe:

Baseline (Observation period in Study 304), Week 12, Week 24, Week 32, Week 40, Week 52 and Week 52 LOCF

End point values	Efficacy Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: Percent Change in Seizure Frequency				
median (full range (min-max))				
Baseline (n=46)	268.2 (79.9 to 22499.4)			
Percent Change in Week 12 (n=45)	-47.7 (-100 to 101.5)			
Percent Change in Week 24 (n= 43)	-48.9 (-97 to 116.6)			
Percent Change in Week 32 (n= 42)	-50.6 (-90.8 to 209.2)			
Percent Change in Week 40 (n= 41)	-52 (-95.5 to 833.2)			
Percent Change in Week 52 (n= 40)	-47.35 (-94.3 to 340.8)			
Percent Change in Week 52 LOCF (n= 46)	-46.3 (-100 to 340.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in the Frequency of Seizures Other than Tonic-Atonic Seizures

End point title	Percent change in the Frequency of Seizures Other than Tonic-Atonic Seizures

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 Weeks, 12, 24, 32, 40, 52 and 52 LOCF 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 frequency, Absence seizure, Atypical absence seizure, Myoclonic seizure, Clonic seizure, Tonic seizure, Tonic-clonic seizure, Atonic seizure, and Unclassified epileptic seizure. This data was based on the diary data collected for 7 days after each visit. Seizure frequency was counted based on the classification established by the ILAE. The diary recorder monitored the participant and recorded the seizure diary in a consistent manner. The Efficacy Analysis Set was used.

End point type	Secondary

End point timeframe:

Baseline (Observation period in Study 304), Week 12, Week 24, Week 32, Week 40, Week 52 and Week 52 LOCF

End point values	Efficacy Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Percent change in seizure frequency				
median (full range (min-max))				
Partial Seizure Week 12 (n=7)	-95 (-100 to 255.6)			
Partial Seizure Week 24 (n=5)	-80.9 (-100 to 303.2)			
Partial Seizure Week 32 (n=5)	-70.5 (-100 to 30.2)			
Partial Seizure Week 40 (n=5)	-85.7 (-100 to -42.4)			
Partial Seizure Week 52 (n=5)	-77.3 (-100 to -61.8)			
Partial Seizure Week 52 LOCF (n=7)	-77.3 (-100 to 189.2)			
Absence Seizure Week 12 (n=1)	-87.7 (-87.7 to -87.7)			
Absence Seizure Week 24 (n=1)	-100 (-100 to -100)			
Absence Seizure Week 32 (n=1)	-100 (-100 to -100)			
Absence Seizure Week 40 (n=1)	-100 (-100 to -100)			
Absence Seizure Week 52 (n=1)	-100 (-100 to -100)			
Absence Seizure Week 52 LOCF (n=1)	-100 (-100 to -100)			
Atypical Absence Seizure Week 12 (n=24)	-86.7 (-100 to 54.7)			
Atypical Absence Seizure Week 24 (n=22)	-92.85 (-100 to 185.7)			
Atypical Absence Seizure Week 32 (n=22)	-92.3 (-100 to 209.2)			
Atypical Absence Seizure Week 40 (n=21)	-100 (-100 to 219.3)			
Atypical Absence Seizure Week 52 (n=21)	-100 (-100 to 737.2)			
Atypical Absence Seizure Week 52 LOCF (n=24)	-100 (-100 to 737.2)			
Myoclonic Seizure Week 12 (n=13)	-100 (-100 to 228.8)			
Myoclonic Seizure Week 24 (n=13)	-100 (-100 to 64.4)			
Myoclonic Seizure Week 32 (n=13)	-100 (-100 to 435.6)			
Myoclonic Seizure Week 40 (n=13)	-100 (-100 to 117.6)			

Myoclonic Seizure Week 52 (n=13)	-100 (-100 to 368.2)			
Myoclonic Seizure Week 52 LOCF (n=14)	-100 (-100 to 368.2)			
Clonic Seizure Week 12 (n=0)	0 (0 to 0)			
Clonic Seizure Week 24 (n=0)	0 (0 to 0)			
Clonic Seizure Week 32 (n=0)	0 (0 to 0)			
Clonic Seizure Week 40 (n=0)	0 (0 to 0)			
Clonic Seizure Week 52 (n=0)	0 (0 to 0)			
Clonic Seizure Week 52 LOCF (n=0)	0 (0 to 0)			
Tonic Seizure Week 12 (n=45)	-35.4 (-100 to 175.2)			
Tonic Seizure Week 24 (n=42)	-37.85 (-100 to 138.5)			
Tonic Seizure Week 32 (n=41)	-49.4 (-100 to 83.5)			
Tonic Seizure Week 40 (n=40)	-47.05 (-100 to 833.2)			
Tonic Seizure Week 52 (n=39)	-36.4 (-100 to 110.2)			
Tonic Seizure Week 52 LOCF (n=45)	-46.2 (-100 to 110.2)			
Tonic-clonic Seizure Week 12 (n=8)	-61.55 (-100 to 300)			
Tonic-clonic Seizure Week 24 (n=7)	-44.1 (-100 to 300)			
Tonic-clonic Seizure Week 32 (n=7)	-22.6 (-100 to 700)			
Tonic-clonic Seizure Week 40 (n=7)	-46.7 (-100 to 1100)			
Tonic-clonic Seizure Week 52 (n=7)	-35.5 (-100 to 700)			
Tonic-clonic Seizure Week 52 LOCF (n=8)	-38.1 (-100 to 700)			
Atonic Seizure Week 12 (n=16)	-60.35 (-100 to 29)			
Atonic Seizure Week 24 (n=15)	-84.3 (-100 to 189.2)			
Atonic Seizure Week 32 (n=14)	-100 (-100 to 20.5)			
Atonic Seizure Week 40 (n=14)	-67.2 (-100 to 261.4)			
Atonic Seizure Week 52 (n=14)	-67.55 (-100 to 526.5)			
Atonic Seizure Week 52 LOCF (n=16)	-67.55 (-100 to 526.5)			
Unclassified Seizure Week 12 (n=1)	-100 (-100 to -100)			
Unclassified Seizure Week 24 (n=1)	6932.3 (6932.3 to 6932.3)			
Unclassified Seizure Week 32 (n=1)	-100 (-100 to -100)			
Unclassified Seizure Week 40 (n=1)	-100 (-100 to -100)			
Unclassified Seizure Week 52 (n=1)	-100 (-100 to -100)			
Unclassified Seizure Week 52 LOCF (n=1)	-100 (-100 to -100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved 100%, 75%, 50% or 25% reduction in Tonic-Atonic Seizure Frequency (Responders)

End point title	Percentage of Participants who Achieved 100%, 75%, 50% or 25% reduction in Tonic-Atonic Seizure Frequency (Responders)

End point description:

Categorized percent change in Tonic-atonic seizure frequency per 28 Days by visit relative to the baseline (Observation Phase in Study 304) was determined based on the diary data collected for 7 days after each visit. The Efficacy Analysis Set was used.

End point type	Secondary

End point timeframe:

Week 12, Week 24, Week 32, Week 40, Week 52 and Week 52 LOCF

End point values	Efficacy Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: Percentage of participants				
number (not applicable)				
Week 12 100% Reduction - Yes	6.5			
Week 12 100% Reduction - No	93.5			
Week 12 75% Reduction - Yes	17.4			
Week 12 75% Reduction - No	82.6			
Week 12 50% Reduction - Yes	43.5			
Week 12 50% Reduction - No	56.5			
Week 12 25% Reduction - Yes	71.7			
Week 12 25% Reduction - No	28.3			
Week 24 100% Reduction - Yes	2.3			
Week 24 100% Reduction - No	97.7			
Week 24 75% Reduction - Yes	11.6			
Week 24 75% Reduction - No	88.4			
Week 24 50% Reduction - Yes	39.5			
Week 24 50% Reduction -No	60.5			
Week 24 25% Reduction - Yes	65.1			
Week 24 25% Reduction - No	34.9			
Week 32 100% Reduction - Yes	2.4			
Week 32 100% Reduction - No	97.6			
Week 32 75% Reduction - Yes	19			
Week 32 75% Reduction - No	81			
Week 32 50% Reduction - Yes	47.6			
Week 32 50% Reduction - No	52.4			

Week 32 25% Reduction - Yes	66.7			
Week 32 25% Reduction - No	33.3			
Week 40 100% Reduction - Yes	4.9			
Week 40 100% Reduction - No	95.1			
Week 40 75% Reduction - Yes	17.1			
Week 40 75% Reduction - No	82.9			
Week 40 50% Reduction - Yes	48.8			
Week 40 50% Reduction - No	51.2			
Week 40 25% Reduction - Yes	61			
Week 40 25% Reduction - No	39			
Week 52 100% Reduction - Yes	5			
Week 52 100% Reduction - No	95			
Week 52 75% Reduction - Yes	20			
Week 52 75% Reduction -No	80			
Week 52 50% Reduction - Yes	37.5			
Week 52 50% Reduction - No	62.5			
Week 52 25% Reduction - Yes	60			
Week 52 25% Reduction - No	40			
Week 52 (LOCF) 100% Reduction - Yes	8.7			
Week 52 (LOCF) 100% Reduction - No	91.3			
Week 52 (LOCF) 75% Reduction - Yes	21.7			
Week 52 (LOCF) 75% Reduction -No	78.3			
Week 52 (LOCF) 50% Reduction - Yes	39.1			
Week 52 (LOCF) 50% Reduction - No	60.9			
Week 52 (LOCF) 25% Reduction - Yes	63			
Week 52 (LOCF) 25% Reduction - No	37			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With An Increase In Tonic-Atonic Seizure Frequency

End point title	Percentage of Participants With An Increase In Tonic-Atonic Seizure Frequency

End point description:

Number of participants with an increase in Tonic-atonic seizure frequency per 28 Days by visit relative to the baseline (Observation Phase in Study 304) was determined based on the diary data collected for 7 days after each visit. The Efficacy Analysis Set was used.

End point type	Secondary

End point timeframe:

Week 12, Week 24, Week 32, Week 40, Week 52 and Week 52 LOCF

End point values	Efficacy Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: Percentage of participants				
number (not applicable)				
Week 12 Increase - Yes	21.7			
Week 12 Increase - No	78.3			
Week 24 Increase - Yes	23.3			
Week 24 Increase - No	76.7			
Week 32 Increase - Yes	16.7			
Week 32 Increase - No	83.3			
Week 40 Increase - Yes	9.8			
Week 40 Increase - No	90.2			
Week 52 Increase - Yes	22.5			
Week 52 Increase -No	77.5			
Week 52 LOCF Increase - Yes	19.6			
Week 52 LOCF Increase - No	80.4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose up to 15 days after the last dose of study treatment, up to approximately 2 year and 9 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Rufinamide

Reporting group description: -

Serious adverse events	Rufinamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 54 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Status epilepticus			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	4 / 54 (7.41%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 54 (1.85%)		
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	Rufinamide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 54 (100.00%)		
Investigations			
Platelet count decreased			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Weight decreased			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	12 / 54 (22.22%)		
occurrences (all)	22		
Skin laceration			

subjects affected / exposed occurrences (all)	5 / 54 (9.26%) 9		
Eyelid injury subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 5		
Fall subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 4		
Mouth injury subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 4		
Nervous system disorders Status epilepticus subjects affected / exposed occurrences (all)	22 / 54 (40.74%) 158		
Somnolence subjects affected / exposed occurrences (all)	14 / 54 (25.93%) 17		
Dizziness subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 4		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	5 / 54 (9.26%) 12		
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 4		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	13 / 54 (24.07%) 27		
Constipation subjects affected / exposed occurrences (all)	9 / 54 (16.67%) 10		

Dental caries subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	7 / 54 (12.96%) 8 6 / 54 (11.11%) 6 4 / 54 (7.41%) 4 3 / 54 (5.56%) 3		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	6 / 54 (11.11%) 9		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 4 3 / 54 (5.56%) 3 3 / 54 (5.56%) 3		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Agitation subjects affected / exposed occurrences (all)	6 / 54 (11.11%) 6 4 / 54 (7.41%) 4		
Infections and infestations Nasopharyngitis			

subjects affected / exposed occurrences (all)	26 / 54 (48.15%) 61		
Influenza subjects affected / exposed occurrences (all)	11 / 54 (20.37%) 15		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 54 (11.11%) 16		
Bronchitis subjects affected / exposed occurrences (all)	5 / 54 (9.26%) 9		
Gastroenteritis subjects affected / exposed occurrences (all)	5 / 54 (9.26%) 5		
Pharyngitis subjects affected / exposed occurrences (all)	4 / 54 (7.41%) 6		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	7 / 54 (12.96%) 7		

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.
05 July 2010	• Clarified the administrations of study treatment during the Conversion Period. • Clarified the dose reduction procedure during the Conversion Period. • Changes made to the clinical trial plan on how blood pressure is taken.
13 October 2010	• Phenobarbital (suppository) was added to rescue drugs for status epilepticus.
11 April 2011	• Newly approved levetiracetam was added to the concomitant antiepileptic drugs which can be used in this study. • Levetiracetam was added to the prohibited antiepileptic drugs for participants under 15 years old, since the drug had not been allowed for patients with <15 years old.
31 October 2011	• Gabapentin was deleted from the prohibited antiepileptic drugs for participants under 15 years old, since the drug was approved for children.
03 April 2012	• Emergency treatment for epilepticus status was revised to include intravenous hyphenytoin as a rescue medication.
24 October 2012	• Revisions made to the Study Design etc. in response to future approval and marketing of the study drug. • Clinical trial was to be considered a post-marketing trial after approval and marketing of the study drug. • End date of the study was defined as the date at which the study drug is on the market and can be prescribed • Assessments at the end of the study are clarified. • Clarified the tapering and end-of-study-assessments those not required for the participants who can continuously use rufinamide after completion of this study. • Instructions were given on how marketed study drug should be handled and delivered to medical institutions for the participants. • Clarification was given on the follow-up of adverse events and serious adverse events. • List of surveys and evaluations the investigators should conduct as the end of the trial. • Clarified the report of pregnancy after use of marketed study drug. • Compliance with Good Post-marketing Study Practice (GPSP) was included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported