Clinical trial results:
An Open-Label Extension Study of Rufinamide Given as Adjunctive Therapy in Patients with Refractory Partial Seizures

Summary

EudraCT number	2016-004950-14
Trial protocol	Outside EU/EEA
Global end of trial date	14 May 2010

Results information

Result version number	v1 (current)
This version publication date	22 June 2019
First version publication date	22 June 2019

Trial information

Trial identification

Sponsor protocol code	E2080-A001-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00448539
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Inc.
Sponsor organisation address	155 Tice Boulevard, Woodcliff Lake, United States, 07677
Public contact	Eisai Medical Information, Eisai Inc., 1 8882472378, esi_oncmedinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., 1 8882472378, esi_oncmedinfo@eisai.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	14 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2010
Global end of trial reached?	Yes
Global end of trial date	14 May 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was an open-label extension study in adolescent and adult (between 12 and 80 years old) subjects who had completed their participation in Study E2080-A001-301. The main objective of this study was to evaluate the safety and efficacy of long-term administration of rufinamide for the control of epileptic seizures in subjects who had refractory partial seizures despite treatment with a maximum of three approved antiepileptic drugs (AEDs).

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 2007
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	Canada: 276
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	286
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)	0
Adolescents (12-17 years)	24
Adults (18-64 years)	252
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed double-blind study E2080-A001-301 were allowed to enter in open-label extension study 302. Subjects completed a 12-day Transition Phase in study301 during which they continued to receive rufinamide at the maintenance dose achieved in study301 (Arm1), or transitioned from placebo to 3200 mg/day, beginning at 800 mg/day (Arm2).

Pre-assignment

Screening details:

Four subjects who intended to enroll from Study 301 to 302 did not enroll and were considered screening failures.

Period 1

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

Blinding implementation details:

Open-label extension study

Arms

Are arms mutually exclusive?	Yes
Arm title	Rufinamide (Rufinamide During Core Study)

Arm description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received rufinamide in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they maintained their 2400 or 3200 mg/day dose. Upon starting the extension study, during the 12-18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

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:

Dose was maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Arm title	Rufinamide (Placebo During Core Study)

Arm description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received placebo in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they transitioned from placebo to 3200 mg/day, beginning at 800 mg/day. Upon starting the extension study, during the 12 to 18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double-blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

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Dosage and administration details:

Dose was maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Number of subjects in period 1	Rufinamide (Rufinamide During Core Study)	Rufinamide (Placebo During Core Study)
Started	134	152
Completed	0	0
Not completed	134	152
Physician decision	67	54
Consent withdrawn by subject	20	24
Diary non-compliance	1	-
Change of medication	2	3
Adverse event, non-fatal	9	26
Medication non-compliance	4	1
Miscellaneous	2	1
Lost to follow-up	1	3
Protocol deviation	1	-
Lack of efficacy	27	40

Baseline characteristics

Reporting groups

Reporting group title	Rufinamide (Rufinamide During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received rufinamide in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they maintained their 2400 or 3200 mg/day dose. Upon starting the extension study, during the 12-18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Reporting group title	Rufinamide (Placebo During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received placebo in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they transitioned from placebo to 3200 mg/day, beginning at 800 mg/day. Upon starting the extension study, during the 12 to 18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double-blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Reporting group values	Rufinamide (Rufinamide During Core Study)	Rufinamide (Placebo During Core Study)	Total
Number of subjects	134	152	286
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)	0	0	0
Adolescents (12-17 years)	6	18	24
Adults (18-64 years)	123	129	252
From 65-84 years	5	5	10
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	63	80	143
Male	71	72	143
Race/Ethnicity, Customized Units: Subjects			
Black	7	13	20
White	115	121	236
Hispanic	10	11	21
Native American	0	2	2
Asian/Pacific Islander	2	2	4
Other	0	3	3

End points

End points reporting groups

Reporting group title	Rufinamide (Rufinamide During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received rufinamide in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they maintained their 2400 or 3200 mg/day dose. Upon starting the extension study, during the 12-18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Reporting group title	Rufinamide (Placebo During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received placebo in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they transitioned from placebo to 3200 mg/day, beginning at 800 mg/day. Upon starting the extension study, during the 12 to 18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double-blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Primary: Percentage Change in Total Partial Seizure Frequency Per 28 Days Relative to the Baseline Phase

End point title	Percentage Change in Total Partial Seizure Frequency Per 28 Days Relative to the Baseline Phase[1]

End point description:

Seizure data was collected via patient diaries. "OL" refers to "open-label." Intent-to-treat (ITT) population: All subjects who completed titration to open-label medication.

End point type	Primary

End point timeframe:

Baseline, Titration Phase (Days 1 to 18), Maintenance Phase

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistcal analyses performed for this end point.

End point values	Rufinamide (Rufinamide During Core Study)	Rufinamide (Placebo During Core Study)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	151		
Units: Percent change				
median (full range (min-max))				
OL Titration Phase	-35.65 (-100 to 1570.7)	-45.1 (-100 to 518.2)		
OL Maintenance Phase	-30.95 (-100 to 246.5)	-31.1 (-100 to 322.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of rufinamide through study termination (up to 3 years and 10 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Rufinamide (Rufinamide During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received rufinamide in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they maintained their 2400 or 3200 mg/day dose. Upon starting the extension study, during the 12-18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Reporting group title	Rufinamide (Placebo During Core Study)

Reporting group description:

Subjects entered this open-label extension study from E2080-A001-301 double-blind core study, where they received placebo in the core study. Prior to starting the extension study, subjects completed a 12-day Transition Phase where they transitioned from placebo to 3200 mg/day, beginning at 800 mg/day. Upon starting the extension study, during the 12 to 18 day open-label Titration Phase, subjects receiving 2400 or 3200 mg/day from the double-blind core study maintained this dose, and subjects who underwent dose reduction in Study E2080-A001-301 titrated from 800 mg/day to 2400 or 3200 mg/day. During the open-ended open-label Maintenance Phase (during which the maximum exposure was 2.9 years), changes in the rufinamide dose were permitted for all subjects; however, the dose must have been maintained within the range of 2400 to 4800 mg/day (i.e., 1200 to 2400 mg twice daily).

Serious adverse events	Rufinamide (Rufinamide During Core Study)	Rufinamide (Placebo During Core Study)	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 134 (21.64%)	23 / 152 (15.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma			

subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			

subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 134 (0.75%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic psychosis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal behaviour			
subjects affected / exposed	1 / 134 (0.75%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			

subjects affected / exposed	1 / 134 (0.75%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
White blood cell count decreased			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug toxicity			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rib fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt malfunction			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	2 / 134 (1.49%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventriculoperitoneal shunt malfunction			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Convulsion			
subjects affected / exposed	5 / 134 (3.73%)	7 / 152 (4.61%)	
occurrences causally related to treatment / all	1 / 5	4 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 134 (0.75%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand Mal Convulsion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures with secondary generalisation			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postictal state			
subjects affected / exposed	0 / 134 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	3 / 134 (2.24%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 134 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal bacteraemia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	0 / 134 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rufinamide (Rufinamide During Core Study)	Rufinamide (Placebo During Core Study)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 134 (65.67%)	114 / 152 (75.00%)	
Investigations			
Weight decreased			
subjects affected / exposed	8 / 134 (5.97%)	9 / 152 (5.92%)	
occurrences (all)	8	10	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	8 / 134 (5.97%)	4 / 152 (2.63%)	
occurrences (all)	12	7	
Fall			
subjects affected / exposed	7 / 134 (5.22%)	5 / 152 (3.29%)	
occurrences (all)	13	7	
Skin laceration			
subjects affected / exposed	9 / 134 (6.72%)	5 / 152 (3.29%)	
occurrences (all)	11	7	
Nervous system disorders			
Convulsion			
subjects affected / exposed	10 / 134 (7.46%)	20 / 152 (13.16%)	
occurrences (all)	10	26	
Coordination Abnormal			
subjects affected / exposed	4 / 134 (2.99%)	10 / 152 (6.58%)	
occurrences (all)	5	13	

Dizziness			
subjects affected / exposed	11 / 134 (8.21%)	43 / 152 (28.29%)	
occurrences (all)	16	65	
Headache			
subjects affected / exposed	15 / 134 (11.19%)	17 / 152 (11.18%)	
occurrences (all)	19	21	
Somnolence			
subjects affected / exposed	2 / 134 (1.49%)	14 / 152 (9.21%)	
occurrences (all)	2	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 134 (4.48%)	15 / 152 (9.87%)	
occurrences (all)	6	20	
Pyrexia			
subjects affected / exposed	1 / 134 (0.75%)	9 / 152 (5.92%)	
occurrences (all)	5	13	
Eye disorders			
Diplopia			
subjects affected / exposed	4 / 134 (2.99%)	10 / 152 (6.58%)	
occurrences (all)	7	14	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 134 (2.99%)	8 / 152 (5.26%)	
occurrences (all)	6	12	
Diarrhoea			
subjects affected / exposed	6 / 134 (4.48%)	9 / 152 (5.92%)	
occurrences (all)	6	9	
Nausea			
subjects affected / exposed	12 / 134 (8.96%)	19 / 152 (12.50%)	
occurrences (all)	12	24	
Vomiting			
subjects affected / exposed	14 / 134 (10.45%)	12 / 152 (7.89%)	
occurrences (all)	15	14	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	2 / 134 (1.49%)	8 / 152 (5.26%)	
occurrences (all)	2	12	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 134 (5.22%)	6 / 152 (3.95%)	
occurrences (all)	7	6	
Depression			
subjects affected / exposed	12 / 134 (8.96%)	3 / 152 (1.97%)	
occurrences (all)	12	3	
Insomnia			
subjects affected / exposed	13 / 134 (9.70%)	10 / 152 (6.58%)	
occurrences (all)	13	10	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 134 (7.46%)	5 / 152 (3.29%)	
occurrences (all)	13	5	
Infections and infestations			
Sinusitis			
subjects affected / exposed	12 / 134 (8.96%)	8 / 152 (5.26%)	
occurrences (all)	15	14	
Upper respiratory tract infection			
subjects affected / exposed	9 / 134 (6.72%)	6 / 152 (3.95%)	
occurrences (all)	11	9	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 134 (1.49%)	11 / 152 (7.24%)	
occurrences (all)	2	13	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated early by the sponsor due to the discontinuation of clinical development for rufinamide.

Notes: