Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Carisbamate as Adjunctive Therapy in Subjects With Partial Onset Seizures, Followed by an Open-Label Extension Study

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2008-007687-41
Trial protocol	LT
Global end of trial date	01 April 2010

Results information

Result version number	v2 (current)
This version publication date	02 June 2016
First version publication date	30 July 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	CARISEPY3013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00740623
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg 30 B-2340 , Beerse, Belgium,
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000360-PIP01-08
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	01 April 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 April 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the effectiveness, safety, and tolerability of carisbamate as add-on therapy for the treatment of partial onset seizures in patients with epilepsy.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. An Independent Data Monitoring Committee (IDMC) was commissioned for the study. Clinical laboratory test (hematology, serum chemistry, and urinalysis). Urine drug and alcohol screens, as well as pregnancy tests were also performed during the study, and serology was performed at baseline, electrocardiogram [ECGs], Vital sign measurements, Physical and neurological examinations and Other safety evaluations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 22
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Croatia: 12
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Hong Kong: 15
Country: Number of subjects enrolled	India: 49
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Lithuania: 12
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Korea, Republic of: 93
Country: Number of subjects enrolled	Russian Federation: 68
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Singapore: 8

Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Taiwan: 28
Country: Number of subjects enrolled	Thailand: 37
Country: Number of subjects enrolled	United States: 52
Worldwide total number of subjects	547
EEA total number of subjects	142

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)	19
Adults (18-64 years)	518
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 600 eligible subjects 16 years of age or older with an established diagnosis of partial onset seizures were to be enrolled in the study.

Pre-assignment

Screening details:

547 participants were assigned into 3 groups in a 1:1:1 ratio to receive either 800 milligram per day [mg/day] carisbamate, 1,200 mg/day carisbamate, or placebo for 14 weeks.

Period 1

Period 1 title	Double-Blind Treatment (Day 1 to 99) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching placebo to carisbamate [CRS] for 14 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for 14 weeks

Arm title	Carisbamate [CRS] 800mg

Arm description:

In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 to 14, the dosage was increase to 800 mg/day.

Arm type	Experimental
Investigational medicinal product name	Carisbamate
Investigational medicinal product code	RWJ-333369
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 to 14, the dosage was increase to 800 mg/day.

Arm title	Carisbamate [CRS] 1200mg

Arm description:

In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 the dosage was increase to 800 mg/day. In Weeks 3 to 14 of the maintenance period, dosage increased to 1,200 mg/day.

Arm type	Experimental

Investigational medicinal product name	Carisbamate
Investigational medicinal product code	RWJ-333369
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 the dosage was increase to 800 mg/day. In Weeks 3 to 14 of the maintenance period, dosage increased to 1,200 mg/day.

Number of subjects in period 1	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg
Started	185	180	182
Completed	164	144	126
Not completed	21	36	56
Consent withdrawn by subject	5	9	9
Adverse event, non-fatal	6	14	30
Other	5	3	6
Adverse event, serious non-fatal	1	3	5
Lost to follow-up	2	1	1
Protocol deviation	2	5	4
Lack of efficacy	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo to carisbamate [CRS] for 14 weeks.	
Reporting group title	Carisbamate [CRS] 800mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 to 14, the dosage was increase to 800 mg/day.	
Reporting group title	Carisbamate [CRS] 1200mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 the dosage was increase to 800 mg/day. In Weeks 3 to 14 of the maintenance period, dosage increased to 1,200 mg/day.	

Reporting group values	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg
Number of subjects	185	180	182
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	4	6	9
Adults (18-64 years)	177	171	170
From 65 to 84 years	4	3	3
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	36.6	36.8	36.8
standard deviation	± 12.18	± 12.02	± 12.53
Title for Gender Units: subjects			
Female	96	92	90
Male	89	88	92

Reporting group values	Total		
Number of subjects	547		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	19		
Adults (18-64 years)	518		
From 65 to 84 years	10		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	278		
Male	269		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Matching placebo to carisbamate [CRS] for 14 weeks.	
Reporting group title	Carisbamate [CRS] 800mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 to 14, the dosage was increase to 800 mg/day.	
Reporting group title	Carisbamate [CRS] 1200mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 milligram per day [mg/day], and in Week 2 the dosage was increase to 800 mg/day. In Weeks 3 to 14 of the maintenance period, dosage increased to 1,200 mg/day.	

Primary: Percent Reduction From Baseline in partial onset Seizure Frequency

End point title	Percent Reduction From Baseline in partial onset Seizure Frequency
End point description:	
The primary efficacy endpoint was the percent reduction in partial onset seizure frequency (average seizure rate per 28 days of all simple partial motor, complex partial, or secondarily generalized seizures) from the baseline phase relative to the entire double-blind treatment phase. The frequency of seizures was calculated by the actual seizure count multiplied by 28, divided by the number of days in the phase; in effect, frequency count was normalized to 28 days.	
End point type	Primary
End point timeframe:	
Baseline up to end of double-blind treatment phase (week 14)	

End point values	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183[1]	176[2]	181[3]	
Units: percent change				
median (full range (min-max))	20.59 (-576 to 100)	29.93 (-1981 to 100)	36.3 (-140 to 100)	

Notes:

[1] - Intent-to-Treat

[2] - Intent-to-Treat

[3] - Intent-to-Treat

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Carisbamate [CRS] 800mg v Placebo

Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.903 [4]
Method	Wilcoxon rank sum test controlling

Notes:

[4] - P-values from Wilcoxon rank sum test controlling for pooled country and enzyme induction group based on IVRS
value.

Statistical analysis title	Statistical analysis 2
Comparison groups	Carisbamate [CRS] 1200mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.041 [5]
Method	Wilcoxon rank sum test controlling

Notes:

[5] - P-values from Wilcoxon rank sum test controlling for pooled country and enzyme induction group based on IVRS
value.

Primary: Number of Participants With greater or equal to 50% reduction in POS frequency from baseline (Responder Rate)

End point title	Number of Participants With greater or equal to 50% reduction in POS frequency from baseline (Responder Rate)

End point description:

End point type	Primary

End point timeframe:

From baseline relative to the entire double-blind treatment phase (14 weeks)

End point values	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183[6]	176[7]	181[8]	
Units: Number of participants	48	49	66	

Notes:

[6] - Intent to treat

[7] - Intent to treat

[8] - Intent to treat

Statistical analyses

Statistical analysis title	Statistical analysis 3
Comparison groups	Carisbamate [CRS] 800mg v Placebo

Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.792
Method	Cochran-Mantel-Haenszel
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.58
upper limit	10.8

Statistical analysis title	Statistical analysis 4
Comparison groups	Carisbamate [CRS] 1200mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.043
Method	Cochran-Mantel-Haenszel
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	19.71

Secondary: Percent Reduction from baseline in Secondarily Generalized Seizure Frequency

End point title	Percent Reduction from baseline in Secondarily Generalized Seizure Frequency

End point description:

Change in secondary generalized seizure frequency is given as a percent reduction computed as:
[Weekly sec. generalized seizure frequency (Baseline)- Weekly sec. generalized seizure frequency (Evaluation Period)]/ [Weekly sec. generalized seizure frequency (Baseline)] x 100.
Positive values in reduction means the value decreased from Baseline during the first 16-week Period.
"Number of participants Analyzed = number of participants who were evaluable for this outcome measure"

End point type	Secondary

End point timeframe:

Baseline up to double-blind treatment phase (14 weeks)

End point values	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78[9]	65[10]	81[11]	
Units: Number of participants				
median (full range (min-max))	11.2 (-800 to 100)	6.7 (-800 to 100)	40 (-800 to 100)	

Notes:

[9] - Intent-to-Treat

[10] - Intent-to-Treat

[11] - Intent-to-Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Onset of Treatment Effect on partial onset seizure frequency reduction

End point title	Time of Onset of Treatment Effect on partial onset seizure frequency reduction

End point description:

Participant's perception of treatment response assessment since the previous visit was noted at each visit. Time to onset of response was calculated in weeks from start of treatment.

End point type	Secondary

End point timeframe:

From baseline relative to the entire double-blind treatment phase (14 weeks)

End point values	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183[12]	176[13]	181[14]	
Units: Number of participants				
median (full range (min-max))	20.97 (-576 to 100)	30.01 (-1981 to 100)	36.26 (-140 to 100)	

Notes:

[12] - Intent-to-Treat

[13] - Intent-to-Treat

[14] - Intent-to-Treat

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1
Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching placebo to CRS for 14 weeks.	
Reporting group title	Carisbamate [CRS] 800mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 Milligram per day [mg/day], and in Week 2 to 14, the dosage was increase to 800 mg/day.	
Reporting group title	Carisbamate [CRS] 1200mg
Reporting group description:	
In Week 1 of the titration period, the dosage of carisbamate was 400 Milligram per day [mg/day], and in Week 2 the dosage was increase to 800 mg/day. In Weeks 3 to 14 of the maintenance period, dosage increased to 1,200 mg/day.	

Serious adverse events	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 184 (3.26%)	9 / 178 (5.06%)	15 / 182 (8.24%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian Epithelial Cancer Metastatic			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	1 / 184 (0.54%)	0 / 178 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver Function Test Abnormal			

subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Intentional Overdose			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist Fracture			
subjects affected / exposed	1 / 184 (0.54%)	0 / 178 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balance Disorder			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Infarction			
subjects affected / exposed	1 / 184 (0.54%)	0 / 178 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical Root Pain			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 184 (0.00%)	2 / 178 (1.12%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dizziness			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Withdrawal Convulsions			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 184 (0.54%)	0 / 178 (0.00%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial Seizures with Secondary Generalisation			
subjects affected / exposed	1 / 184 (0.54%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 184 (0.00%)	2 / 178 (1.12%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food Poisoning			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vomiting			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 184 (0.54%)	1 / 178 (0.56%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 178 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Carisbamate [CRS] 800mg	Carisbamate [CRS] 1200mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 184 (39.67%)	105 / 178 (58.99%)	109 / 182 (59.89%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	17 / 184 (9.24%)	52 / 178 (29.21%)	58 / 182 (31.87%)
occurrences (all)	25	82	85
Headache			
subjects affected / exposed	31 / 184 (16.85%)	32 / 178 (17.98%)	43 / 182 (23.63%)
occurrences (all)	58	64	89
Somnolence			
subjects affected / exposed	19 / 184 (10.33%)	22 / 178 (12.36%)	28 / 182 (15.38%)
occurrences (all)	20	24	30
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 184 (9.24%)	14 / 178 (7.87%)	18 / 182 (9.89%)
occurrences (all)	18	16	18
Eye disorders			
Diplopia			
subjects affected / exposed	3 / 184 (1.63%)	9 / 178 (5.06%)	14 / 182 (7.69%)
occurrences (all)	4	19	22
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	15 / 184 (8.15%)	11 / 178 (6.18%)	23 / 182 (12.64%)
occurrences (all)	24	15	25
Vomiting			
subjects affected / exposed	4 / 184 (2.17%)	9 / 178 (5.06%)	8 / 182 (4.40%)
occurrences (all)	4	10	8
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 184 (1.63%)	9 / 178 (5.06%)	4 / 182 (2.20%)
occurrences (all)	3	11	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 184 (2.72%)	6 / 178 (3.37%)	12 / 182 (6.59%)
occurrences (all)	5	8	12
Metabolism and nutrition disorders			

Decreased Appetite subjects affected / exposed occurrences (all)	5 / 184 (2.72%) 5	9 / 178 (5.06%) 12	5 / 182 (2.75%) 5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2009	Description Added a definition in the 'other important medical event" category to indicate that suspected transmission of an infectious agent by a medicinal product was considered a serious adverse event. The statistical procedures section was modified to indicate that physical and neurologic examination results were to be analyzed by tabulation of abnormal results, not by change from baseline at each time point. The section on the use of concomitant AEDs was updated to clarify the criteria for inadequate response to prior AEDs, and indicate that participants with a history of 10 or more generalized seizures (of any type) per month must have exhibited inadequate response to at least 3 prior AEDs. Additional clarifications were made to the Prohibitions and Restrictions, and to the Pre-study and Concomitant The Study Protocol was also updated to specify that participant who could tolerate the dosage during the first week of the titration period, or who could not tolerate a dosage reduction during Weeks 2 through 4 as a result of side effects, were to be withdrawn from the study. Finally, the sections on Laboratory Tests, and ECG collection, were clarified to remove serum pregnancy testing (only urine pregnancy tests to be performed). The pregnancy test was added for Visit 3 (Day 1). A second ECG reading was made at visit 3 (baseline). The visit window for Visits X1 to X3 of study was changed from 2 weeks to 3 days. The statistical step-down procedure was modified for both the primary and secondary efficacy endpoints. The step-down procedure was planned to ensure the type I error rate due to multiple treatment comparisons was controlled at the 0.05 level. First, the carisbamate 800-mg/day and 1200 -mg/day dosage groups were be combined as a single group, and the combined carisbamate group compared with the placebo group for the endpoint.
22 September 2009	A change was made to specify that participants currently receiving double-blind study medication, or who have been receiving carisbamate in the extension phase for less than 6 weeks, must be withdrawn from the study if they experience during the study, or have a history (at any time in their life) of Stevens Johnson Syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, a drug-related exfoliative rash, any drug-related rash requiring hospitalization, or rash associated with an AED that involved conjunctiva or mucosae, or a maculopapular rash that required discontinuation of an antiepileptic drug [AED]. Finally an amendment was made to specify that enrolled participants who concurrently develop two or more of the following signs and symptoms should be withdrawn from the study, unless these are clearly attributable to another documented illness (e.g.,infectious pneumonia): rash; fever (Less than [>] 38.5ºC); lymphadenopathy (must have either enlargement of nodes relative to baseline, or tenderness); eosinophilia (absolute eosinophil count greater or equal to 700/microliter, or, if elevated at baseline, an increase of more than 50%); alanine aminotransferase [ALT] greater than 2 times the upper limit of normal (ULN), confirmed by a repeat measurement; signs or symptoms of significant pulmonary, cardiac, renal, muscular or pancreatic involvement.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported