Clinical trial results:
A Randomized, Double-Blind, Parallel-Group, Multicenter Study to Evaluate the Retention Rate, Efficacy, Safety, and Tolerability of Carisbamate, Topiramate and Levetiracetam as Adjunctive Therapy in Subjects With Partial Onset Seizures

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

Summary

EudraCT number	2007-002929-78
Trial protocol	GB CZ BE FI FR IT ES PT
Global end of trial date	09 May 2010

Results information

Result version number	v2 (current)
This version publication date	02 June 2016
First version publication date	01 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	CARISEPY3007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00563459
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ortho-McNeil Janssen Scientific Affairs, LLC
Sponsor organisation address	1125 Trenton-Harbourton Road, Titusville, NJ 08560, United States,
Public contact	Ortho-McNeil Janssen Scientific Affairs, LLC, Ortho-McNeil Janssen Scientific Affairs, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Ortho-McNeil Janssen Scientific Affairs, LLC, Ortho-McNeil Janssen Scientific Affairs, LLC, ClinicalTrialsEU@its.jnj.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	09 May 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 May 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the long-term retention rate of carisbamate (CRS) versus topiramate (TPM) and levetiracetam (LEV) when given adjunctively to subjects with partial onset seizures based on discontinuations due to all causes over a 6-month period.

Protection of trial subjects:

An independent Data Safety Monitoring Board (DSMB) met during the course of the study to ensure the safety of the subjects and monitor any clinically relevant trends. Safety and tolerability evaluations included monitoring of the frequency, severity, and timing of adverse events (AEs), clinical laboratory test values, liver function tests, serum lipid profiles, urine drug screen, 12-lead electrocardiogram (ECG) recordings, vital signs measurements, physical and neurologic examinations, study drug levels and concomitant adjunctive antiepileptic drug (AED) levels, and pregnancy tests for females of childbearing potential.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2007
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	Czech Republic: 4
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	89
EEA total number of subjects	24

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)	2
Adults (18-64 years)	84
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 600 subjects were to be enrolled (200 subjects in each group) initially. At study termination, 89 subjects had been randomly assigned to treatment (29, 29, and 31 subjects in the CRS versus TPM and LEV groups, respectively).

Pre-assignment

Screening details:

Across all treatment groups, of the 89 subjects who were randomly assigned to treatment and received at least 1 dose of study drug, 60 subjects completed the 6-month core double-blind phase (17 CRS, 19 TPM, and 24 LEV) and 5 subjects (2 CRS, 2 TPM, and 1 LEV) completed the 12-month double-blind phase; Only 9 subjects had begun the open-label phase.

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Carisbamate

Arm description:

The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day).

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

Dosage and administration details:

The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 mg/day.

Arm title	Topiramate

Arm description:

The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.

Arm type	Active comparator
Investigational medicinal product name	Topiramate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.

Arm title	Levetiracetam

Arm description:

The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.

Arm type	Active comparator

Investigational medicinal product name	levetiracetam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.

Number of subjects in period 1	Carisbamate	Topiramate	Levetiracetam
Started	29	29	31
Completed	2	2	1
Not completed	27	27	30
Consent withdrawn by subject	4	4	-
Adverse event, non-fatal	-	4	2
Non compliance	-	-	2
Insufficient seizure control	5	1	2
Lost to follow-up	-	2	-
Discontinuation due to early termination of study	18	16	24

Baseline characteristics

Reporting groups	
Reporting group title	Carisbamate
Reporting group description:	
The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day).	
Reporting group title	Topiramate
Reporting group description:	
The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.	
Reporting group title	Levetiracetam
Reporting group description:	
The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.	

Reporting group values	Carisbamate	Topiramate	Levetiracetam
Number of subjects	29	29	31
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	28	27	29
From 65 to 84 years	1	1	1
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	37.9	38.3	39.8
standard deviation	± 11.82	± 15.12	± 13.11
Title for Gender			
Units: subjects			
Female	18	10	15
Male	11	19	16

Reporting group values	Total		
Number of subjects	89		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	2		
Adults (18-64 years)	84		
From 65 to 84 years	3		
85 years and over	0		
Title for AgeContinuous			
Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender			
Units: subjects			
Female	43		
Male	46		

End points

End points reporting groups

Reporting group title	Carisbamate
Reporting group description:	
The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day).	
Reporting group title	Topiramate
Reporting group description:	
The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.	
Reporting group title	Levetiracetam
Reporting group description:	
The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.	

Primary: Time From the First Intake of Study Medication to Discontinuation (all causes) of Study Medication During the 6 Month Core Double-Blind Phase

End point title	Time From the First Intake of Study Medication to Discontinuation (all causes) of Study Medication During the 6 Month Core Double-Blind Phase[1]
End point description:	
Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.	
End point type	Primary
End point timeframe:	
Baseline up to month 6	

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Days				
median (full range (min-max))	(to)	(to)	(to)	

Notes:

[2] - Due to early termination, no subject was analyzed for this endpoint.

[3] - Due to early termination, no subject was analyzed for this endpoint.

[4] - Due to early termination, no subject was analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Reasons For Discontinuation

End point title	Number of Subjects With Reasons For Discontinuation
End point description:	
Randomized analysis set included all subjects who received at least 1 dose of study drug.	
End point type	Secondary

End point timeframe:

Month 6 and 12

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	31	
Units: Number				
Insufficient seizure control	5	1	2	
Adverse event	0	4	2	
Non-compliance	0	0	2	
Lost to follow-up	0	2	0	
Subject choice (subject withdrew consent)	4	4	0	
Pregnancy	0	0	0	
Death	0	0	0	
Other	18	16	24	
No. of subjects completed double blind phase	2	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Seizures Rates Among the 3 Treatment Arms

End point title	Number of Subjects with Seizures Rates Among the 3 Treatment Arms

End point description:

Safety analysis set included all subjects who were randomized and received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Upto 12 months

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	31	
Units: Subjects				
arithmetic mean (standard deviation)				
Simple partial motor	1.5 (± 3)	0.73 (± 2.85)	2.4 (± 6.78)	
Complex partial	1.92 (± 2.79)	0.94 (± 1.81)	1.25 (± 2.95)	
Partial evolving to secondarily generalized	0.44 (± 0.99)	0.49 (± 1.78)	0.24 (± 0.74)	
Other	0.01 (± 0.06)	0.16 (± 0.75)	0.69 (± 3.84)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cognitive Disorders With a Computorized Cognitive Test Battery Among the 3 Treatment Arms

End point title	Change From Baseline in Cognitive Disorders With a Computorized Cognitive Test Battery Among the 3 Treatment Arms

End point description:

Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.

End point type	Secondary

End point timeframe:

Baseline; Week 3, 7; Month 3, 6

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[5] - Due to early termination, no subject was analyzed for this endpoint.

[6] - Due to early termination, no subject was analyzed for this endpoint.

[7] - Due to early termination, no subject was analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Neuropsychiatric side effect profiles of Carisbamate (CRS) and levetiracetam (LEV)

End point title	Neuropsychiatric side effect profiles of Carisbamate (CRS) and levetiracetam (LEV)

End point description:

Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.

End point type	Secondary

End point timeframe:

Month 6 and 12

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[8] - Due to early termination of study, no subject was analyzed in this endpoint.

[9] - Due to early termination of study, no subject was analyzed in this endpoint.

[10] - Due to early termination of study, no subject was analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reported Cognitive and Psychiatric Disorders Among the 3 Treatment Arms Recorded as Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects Reported Cognitive and Psychiatric Disorders Among the 3 Treatment Arms Recorded as Treatment Emergent Adverse Events (TEAEs)

End point description:

TEAEs in the double-blind phase are adverse events which started on or after the start of double-blind treatment and before the start of transition or open-label treatment, or within 14 days (30 days if serious) of the last dose of double-blind study drug if the subject did not take transition or open-label study drug. Safety analysis set included subjects who were randomly assigned to treatment and received at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Month 6 and 12

End point values	Carisbamate	Topiramate	Levetiracetam	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	29	31	
Units: subjects				
Cognitive disorder	0	2	0	
Psychiatric disorder	3	4	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 30 days after last dose of study drug	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0
Reporting groups	
Reporting group title	Carisbamate
Reporting group description: The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 mg/day	
Reporting group title	Levetiracetam
Reporting group description: The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day	
Reporting group title	Topiramate
Reporting group description: The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day	

Serious adverse events	Carisbamate	Levetiracetam	Topiramate
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	3 / 31 (9.68%)	1 / 29 (3.45%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Brain Contusion			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral Neck Fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (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
Muscle Strain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (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
Cardiac disorders			

Cardio-Respiratory Arrest			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (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
Nervous system disorders			
Cerebral Haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (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
Epilepsy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (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			
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (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

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Carisbamate	Levetiracetam	Topiramate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 29 (68.97%)	27 / 31 (87.10%)	24 / 29 (82.76%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin Papilloma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Chills			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	3 / 29 (10.34%)	3 / 31 (9.68%)	3 / 29 (10.34%)
occurrences (all)	4	3	3
Gait Disturbance			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Influenza Like Illness			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	0	2	1
Irritability			
subjects affected / exposed	1 / 29 (3.45%)	4 / 31 (12.90%)	1 / 29 (3.45%)
occurrences (all)	1	4	1
Oedema Peripheral			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Allergic Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 31 (6.45%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Pulmonary Congestion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Rhinitis Seasonal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	0 / 29 (0.00%)	2 / 31 (6.45%)	1 / 29 (3.45%)
occurrences (all)	0	2	1
Aggression			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	1 / 29 (3.45%)	2 / 31 (6.45%)	1 / 29 (3.45%)
occurrences (all)	1	2	2
Anxiety			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Apathy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Depressive Symptom			

subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Hallucination			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Hostility			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Nightmare			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Sleep Disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 31 (6.45%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Body Temperature Increased			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	2	1	0
Electrocardiogram T Wave Inversion			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Liver Function Test Abnormal			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Neutrophil Count Decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Urine Analysis Abnormal			

subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Weight Decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	4 / 29 (13.79%)
occurrences (all)	0	0	4
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Back Injury			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Ligament Rupture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Skin Laceration			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Stress Fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Bradycardia			

subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Extrasystoles			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Cognitive Disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Balance Disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Disturbance in Attention			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Dizziness			
subjects affected / exposed	6 / 29 (20.69%)	4 / 31 (12.90%)	5 / 29 (17.24%)
occurrences (all)	8	4	5
Dizziness Postural			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	7 / 29 (24.14%)	6 / 31 (19.35%)	6 / 29 (20.69%)
occurrences (all)	26	7	16
Hypersomnia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2

Hypokinesia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Memory Impairment			
subjects affected / exposed	2 / 29 (6.90%)	2 / 31 (6.45%)	2 / 29 (6.90%)
occurrences (all)	3	2	2
Mental Impairment			
subjects affected / exposed	0 / 29 (0.00%)	2 / 31 (6.45%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Myoclonus			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Paraesthesia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	8 / 29 (27.59%)
occurrences (all)	0	0	13
Psychomotor Hyperactivity			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	6 / 29 (20.69%)	11 / 31 (35.48%)	3 / 29 (10.34%)
occurrences (all)	6	11	3
Speech Disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	3 / 29 (10.34%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Eye Haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Eye Pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Photophobia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Vision Blurred			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Visual Acuity Reduced			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Breath Odour			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Abdominal Pain Upper			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			

subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Dry Mouth			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Gingival Bleeding			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Gingival Swelling			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	2 / 29 (6.90%)	1 / 31 (3.23%)	4 / 29 (13.79%)
occurrences (all)	2	2	4
Oral Discomfort			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Umbilical Hernia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 31 (6.45%)	0 / 29 (0.00%)
occurrences (all)	1	2	0
Granuloma Annulare			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pain of Skin			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Hypoaesthesia Facial			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	3
Rash			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 29 (6.90%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
Back Pain			
subjects affected / exposed	2 / 29 (6.90%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	2	1	0
Mobility Decreased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Muscular Weakness			
subjects affected / exposed	2 / 29 (6.90%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal Pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	3
Myalgia			

subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Pain in Extremity			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Cellulitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Ear Infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Genitourinary Tract Infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Herpes Simplex			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	3 / 29 (10.34%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	3	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 29 (3.45%)	3 / 31 (9.68%)	2 / 29 (6.90%)
occurrences (all)	2	3	2
Skin Infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Tooth Abscess			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1

Urinary Tract Infection			
subjects affected / exposed	3 / 29 (10.34%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	3	1	0
Viral Infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	6	0	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	3 / 29 (10.34%)
occurrences (all)	0	0	3
Decreased Appetite			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Increased Appetite			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2008	The following changes were made in Amendment INT-1: increased CRS target dosage from 400 to 800 mg/day and dosage range changed from 300 to 400 mg/day to 400 to 1,200 mg/day; revised CRS titration schedule to 400 mg/day starting at Week 1 and 800 mg/day starting at Week 2; changed open-label carisbamate (CRS) dosages from 200 to 400 mg/day to 400 to 1,200 mg/day; increased the maximum allowable dosages of each comparator group (TPM: from 300 to 400 mg/day, LEV: from 2,000 to 3,000 mg/day) to be consistent with their respective prescribing information; removed provision that allowed one dosage adjustment during the double-blind maintenance period to reduce unpredictability that may be associated with a change in study drug dosage and to allow better interpretation of the retention rates in the maintenance period, clarified procedures for the double-blind titration period, double-blind maintenance phase, transition phase, double-blind exit phase, and open-label phase, revised objectives, hypothesis, inclusion and exclusion criteria, computerized cognitive test battery, statistical methods, and pharmacogenomics , added/updated algorithms for monitoring liver function tests and for ECG monitoring of the QT interval corrected for heart rate using Fridericia formula (QTcF) interval.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 January 2010	Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.	-

Notes:

Limitations and caveats

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

With limitations of low enrollment of subjects per treatment arm and early termination of the study by the sponsor, primary efficacy analysis was not performed and the focus of this report was safety. Safety data should be interpreted cautiously.

Notes: