



Clinical trial results:

A Double-blind Trial Comparing the Efficacy, Tolerability and Safety of Monotherapy Topiramate Versus Phenytoin in Subjects With Seizures Indicative of New Onset Epilepsy

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

Summary

EudraCT number	2015-001222-42
Trial protocol	Outside EU/EEA
Global end of trial date	06 August 2007

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	31 July 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set• Review of data

Trial information

Trial identification

Sponsor protocol code	CAPSS-272
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00210782
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Pharmaceutical Research and Development
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333CM
Public contact	Clinical Registry Group-JB BV, Johnson & Johnson Pharmaceutical Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group-JB BV, Johnson & Johnson Pharmaceutical Research and Development, 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	06 August 2007
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to compare the effectiveness and safety of two treatment regimens, topiramate as compared to phenytoin, in preventing seizures in subjects with new-onset epilepsy who require rapid initiation of antiepileptic drug therapy. The purpose of the Open-Label Extension Phase of the study was to evaluate the efficacy, tolerability, and safety of monotherapy topiramate during the 12-week Open-Label Extension Phase in subjects who completed the Double-Blind Phase of the study or who exited the Double-Blind Phase of the study due to seizure.

Protection of trial subjects:

Safety evaluations for this study included monitoring of adverse events, clinical laboratory tests (hematology, serum chemistry and urinalysis), vital sign measurements, physical and neurological examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2004
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	United States: 261
Worldwide total number of subjects	261
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)	29
Adults (18-64 years)	221
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 261 subjects who were randomized into the study 133 subjects received topiramate and 128 received phenytoin. Overall, 217 subjects (83.1%) completed the Double-Blind Phase of the study.

Period 1

Period 1 title	Baseline Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Topiramate

Arm description:

The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.

Arm type	Experimental
Investigational medicinal product name	TOPAMAX
Investigational medicinal product code	
Other name	TOPIRAMATE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.

Arm title	Phenytoin
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Arm description:

The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.

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

Dosage and administration details:

The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.

Number of subjects in period 1	Topiramate	Phenytoin
Started	128	126
Completed	128	126

Period 2

Period 2 title	Double Blind
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Topiramate

Arm description:

The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.

Arm type	Experimental
Investigational medicinal product name	TOPAMAX
Investigational medicinal product code	
Other name	TOPIRAMATE
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.

Arm title	Phenytoin
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Arm description:

The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.

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

Dosage and administration details:

The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.

Number of subjects in period 2	Topiramate	Phenytoin
Started	133	128
Completed	116	101
Not completed	17	27
Consent withdrawn by subject	4	2
Adverse event, non-fatal	7	14
Other	3	7
Adverse event, serious	1	2
Lost to follow-up	2	2

Baseline characteristics

Reporting groups^[1]

Reporting group title	Topiramate
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Reporting group description:

The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.

Reporting group title	Phenytoin
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Reporting group description:

The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period

Reporting group values	Topiramate	Phenytoin	Total
Number of subjects	128	126	254
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	15	14	29
Adults (18-64 years)	109	105	214
From 65 to 84 years	4	7	11
85 years and over	0	0	0
Title for AgeContinuous Units: Years			
arithmetic mean	33.3	35.1	-
standard deviation	± 14.2	± 15.37	-
Title for Gender Units: subjects			
Female	78	55	133
Male	50	71	121

Subject analysis sets

Subject analysis set title	Double Blind ITT (Intent-to-treat) Analysis Set - Topiramate
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

ITT Population is defined as all randomized subjects who received at least one dose of study drug and had at least one post-randomization efficacy measurement.

Subject analysis set title	Double Blind ITT (Intent-to-treat) Analysis Set - Phenytoin
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

ITT Population is defined as all randomized subjects who received at least one dose of study drug and had at least one post-randomization efficacy measurement.

Reporting group values	Double Blind ITT (Intent-to-treat) Analysis Set - Topiramate	Double Blind ITT (Intent-to-treat) Analysis Set - Phenytoin	
Number of subjects	128	126	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	15	14	
Adults (18-64 years)	109	105	
From 65 to 84 years	4	7	
85 years and over	0	0	
Title for AgeContinuous Units: Years			
arithmetic mean	33.3	35.1	
standard deviation	± 14.2	± 15.37	
Title for Gender Units: subjects			
Female	78	55	
Male	50	71	

End points

End points reporting groups

Reporting group title	Topiramate
Reporting group description: The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.	
Reporting group title	Phenytoin
Reporting group description: The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.	
Reporting group title	Topiramate
Reporting group description: The initiation dose on Day 1 for topiramate-randomized subjects was 100 milligram (mg), administered orally as an initial dose of 50 mg of topiramate, followed by two successive doses of 25 mg each administered at 2-hour intervals.	
Reporting group title	Phenytoin
Reporting group description: The initiation dose on Day 1 for phenytoin-randomized subjects was 1,000 mg, administered orally as an initial dose of 400 mg of phenytoin, followed by two successive doses of 300 mg each administered at 2-hour intervals.	
Subject analysis set title	Double Blind ITT (Intent-to-treat) Analysis Set - Topiramate
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT Population is defined as all randomized subjects who received at least one dose of study drug and had at least one post-randomization efficacy measurement.	
Subject analysis set title	Double Blind ITT (Intent-to-treat) Analysis Set - Phenytoin
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT Population is defined as all randomized subjects who received at least one dose of study drug and had at least one post-randomization efficacy measurement.	

Primary: Time to First Seizure During The Double Blind Phase

End point title	Time to First Seizure During The Double Blind Phase
End point description: Efficacy analysis set included all ITT subjects who received at least 1 dose of study drug and had at least 1 post-randomization efficacy measurement.	
End point type	Primary
End point timeframe: Day 1 up to Day 28	

End point values	Topiramate	Phenytoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: days				
arithmetic mean (standard error)	25.4 (± 0.61)	24.8 (± 0.44)		

Statistical analyses

Statistical analysis title	Wald Chi square
Statistical analysis description:	
Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with time to first seizure.	
Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3661
Method	Wald Chi-squared

Secondary: Effect of sex, age, Baseline Weight, Baseline Seizure Type, and Duration Since First Diagnosis of Epilepsy on the Time to Seizure

End point title	Effect of sex, age, Baseline Weight, Baseline Seizure Type, and Duration Since First Diagnosis of Epilepsy on the Time to Seizure
End point description:	
Efficacy analysis set included all ITT subjects who received at least 1 dose of study drug and had at least 1 post-randomization efficacy measurement. No descriptive data was planned to be analyzed for this endpoint. Thus NA (Not applicable)= +/-9999	
End point type	Secondary
End point timeframe:	
Day 1 up to Day 28	

End point values	Topiramate	Phenytoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: ratio				
arithmetic mean (standard error)				
Effect of Sex	-99999 (± 99999)	-99999 (± 99999)		
Effect of Age	-99999 (± 99999)	-99999 (± 99999)		
Effect of Baseline Weight	-99999 (± 99999)	-99999 (± 99999)		
Effect of Generalized Tonic-Clonic Seizures	-99999 (± 99999)	-99999 (± 99999)		
Effect of Complex Partial Seizure	-99999 (± 99999)	-99999 (± 99999)		

Effect of Simple Partial Seizure	-99999 (± 99999)	-99999 (± 99999)		
Effect of Absence Seizures	-99999 (± 99999)	-99999 (± 99999)		
Effect of Myoclonic Seizures	-99999 (± 99999)	-99999 (± 99999)		
Effect of Other Seizures	-99999 (± 99999)	-99999 (± 99999)		
Duration Since First Diagnosis of Epilepsy	-99999 (± 99999)	-99999 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1: Wald Chi square
Statistical analysis description: Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with sex.	
Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8021
Method	Wald Chi-squared

Statistical analysis title	Statistical Analysis 2: Wald Chi square
Statistical analysis description: Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with age.	
Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7616
Method	Wald Chi-squared

Statistical analysis title	Statistical Analysis 3: Wald Chi square
Statistical analysis description: Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with baseline weight	
Comparison groups	Topiramate v Phenytoin

Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5147
Method	Wald Chi-squared

Statistical analysis title	Statistical Analysis 4: Wald Chi square
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Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with generalized tonic-clonic seizure.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9353
Method	Wald Chi-squared

Statistical analysis title	Statistical Analysis 5: Wald Chi Square
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Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with complex partial seizure.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.063
Method	Wald Chi-squared

Statistical analysis title	Statistical Analysis 6: Wald Chi Square
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Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with simple partial seizure.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7094
Method	Wald Chi-square

Statistical analysis title	Statistical Analysis 7: Wald Chi Square
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Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with absence seizure.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9899
Method	Wald Chi-squared

Statistical analysis title

Statistical Analysis 8: Wald Chi Square

Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with myoclonic seizure.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5001
Method	Wald Chi-squared

Statistical analysis title

Statistical Analysis 9: Wald Chi Square

Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with other seizure type.

Comparison groups	Topiramate v Phenytoin
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9947
Method	Wald Chi-squared

Statistical analysis title

Statistical Analysis 10: Wald Chi Square

Statistical analysis description:

Inferential Tests for treatment difference in time to first seizure by exiting seizure type during the double-blind phase was analyzed using Wald test from Cox proportional hazard model with duration since first diagnosis of epilepsy on the time to seizure.

Comparison groups	Topiramate v Phenytoin
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Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7131
Method	Wald Chi-squared

Secondary: Proportion of Subjects who Were Seizure-Free at Day 28

End point title	Proportion of Subjects who Were Seizure-Free at Day 28
End point description:	Efficacy analysis set included all ITT subjects who received at least 1 dose of study drug and had at least 1 post-randomization efficacy measurement.
End point type	Secondary
End point timeframe:	Day 28

End point values	Topiramate	Phenytoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: subjects	92	87		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Seizure by Seizure Type

End point title	Time to First Seizure by Seizure Type
End point description:	Time to first seizure by seizure type was calculated Kaplan-Meier estimates for the ITT Population for each treatment group. Efficacy analysis set included all ITT subjects who received at least 1 dose of study drug and had at least 1 post-randomization efficacy measurement.
End point type	Secondary
End point timeframe:	Day 1 up to Day 28

End point values	Topiramate	Phenytoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: days				
arithmetic mean (standard error)				
Time to First Generalized Tonic-Clonic Seizure	24.3 (± 0.34)	25.9 (± 0.1)		

Time to First Complex Partial Seizure	26.3 (± 0.52)	23.9 (± 0.42)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Seizures Observed During the Double Blind Phase

End point title	Incidence of Seizures Observed During the Double Blind Phase
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End point description:

The proportion of subjects who experienced GTC or complex partial seizures, GTC seizures, complex partial seizures and seizures of all types were observed during the double blind phase of the study. Efficacy analysis set included all ITT subjects who received at least 1 dose of study drug and had at least 1 post-randomization efficacy measurement.

End point type	Secondary
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End point timeframe:

Day 1 up to Day 28

End point values	Topiramate	Phenytoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: Number				
arithmetic mean (standard deviation)				
GTC or Complex Partial Seizures	0.4 (± 1.3)	0.2 (± 0.8)		
Generalized tonic-clonic seizures	0.1 (± 0.56)	0.1 (± 0.29)		
Complex Partial Seizures	0.3 (± 1.21)	0.2 (± 0.75)		
Seizures of all Types	0.5 (± 1.33)	0.3 (± 0.87)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Day 49

Assessment type	Non-systematic
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Dictionary used

Dictionary name	WHOART
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Dictionary version	1992
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Reporting groups

Reporting group title	Topiramate
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Reporting group description:

Topiramate

Reporting group title	Phenytoin
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Reporting group description:

Phenytoin

Serious adverse events	Topiramate	Phenytoin	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 132 (1.52%)	5 / 127 (3.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Cerebrovascular Disorder			
subjects affected / exposed	0 / 132 (0.00%)	1 / 127 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	0 / 132 (0.00%)	1 / 127 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsions Grand Mal			
subjects affected / exposed	1 / 132 (0.76%)	0 / 127 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	0 / 132 (0.00%)	1 / 127 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Syncope			
subjects affected / exposed	1 / 132 (0.76%)	0 / 127 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 132 (0.00%)	2 / 127 (1.57%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide Attempt			
subjects affected / exposed	0 / 132 (0.00%)	1 / 127 (0.79%)	
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	Topiramate	Phenytoin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 132 (58.33%)	72 / 127 (56.69%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	26 / 132 (19.70%)	35 / 127 (27.56%)	
occurrences (all)	34	36	
Paraesthesia			
subjects affected / exposed	29 / 132 (21.97%)	5 / 127 (3.94%)	
occurrences (all)	37	5	
Headache			
subjects affected / exposed	11 / 132 (8.33%)	15 / 127 (11.81%)	
occurrences (all)	14	17	
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	12 / 132 (9.09%) 12	11 / 127 (8.66%) 12	
Eye disorders Vision Abnormal subjects affected / exposed occurrences (all)	6 / 132 (4.55%) 6	9 / 127 (7.09%) 10	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	9 / 132 (6.82%) 9	12 / 127 (9.45%) 14	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 132 (0.76%) 1	9 / 127 (7.09%) 9	
Psychiatric disorders Confusion subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Difficulty with Concentration/Attention subjects affected / exposed occurrences (all) Nervousness subjects affected / exposed occurrences (all)	8 / 132 (6.06%) 8 16 / 132 (12.12%) 19 8 / 132 (6.06%) 8 7 / 132 (5.30%) 8	2 / 127 (1.57%) 3 18 / 127 (14.17%) 19 3 / 127 (2.36%) 3 2 / 127 (1.57%) 2	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	9 / 132 (6.82%) 9	7 / 127 (5.51%) 7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2005	Amendment 1 provided specific criteria for acceptable benzodiazepine use, added text specifying visit windows, and provided details about follow-up for subjects who exited due to a complex partial or GTC seizure, about taper for subjects not entering the Open-Label Extension Phase, and about returned study drug.
31 May 2006	Amendment 2 included the following changes: Change in the primary analysis model, allowing a decrease in the sample size from 310 subjects (155 per treatment group) to 262 subjects (131 per treatment group); change in primary efficacy analysis for the Double-Blind Phase from Kaplan-Meier estimates of the cumulative rate of time to the first seizure to a non-inferiority log-rank test for the equivalence of 2 seizure-free survival curves; allow subjects with a positive tetrahydrocannabinol (THC) at screening to enter the study, establishment of independent data monitoring committee (IDMC), procedure to allow subjects to receive a prescription for topiramate at the end of the Open-Label Extension Phase, since topiramate had been approved for monotherapy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported