Clinical trial results:
Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Oxcarbazepine Extended-Release (OXC XR) as Adjunctive Therapy in Subjects with Refractory Partial Epilepsy on up to Three Concomitant Anti-epileptic Medications

Summary

EudraCT number	2008-003334-19
Trial protocol	BG
Global end of trial date	30 November 2011

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	804P302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00908349
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Supernus Pharmaceuticals, Inc.
Sponsor organisation address	9715 Key West Avenue, Rockville, MD, United States, 20850
Public contact	Jonathan Rubin, MD, Supernus Pharmaceuticals, Inc., jrubin@supernus.com
Scientific contact	Joseph T. Hull, PhD, Supernus Pharmaceuticals, Inc., jhull@supernus.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 June 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2011
Global end of trial reached?	Yes
Global end of trial date	30 November 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety and tolerability of long-term administration of adjunctive oxcarbazepine extended-release (OXC XR) in the treatment of seizures of partial origin in adult subjects with refractory epilepsy receiving up to three concomitant anti-epileptic drugs (AEDs).

Protection of trial subjects:

All potential study participants provided informed consent. Subjects who completed the randomized, double-blind, placebo-control trial (804P301) and who continued to meet the inclusion/exclusion criteria were eligible to participate for this open-label extension (OLE) safety trial (804P302). Eligible subjects who enrolled and received study medication in this OLE trial were monitored for safety and tolerability throughout the study. During treatment at study visits and/or at the end of study (or early discontinuation) visit, the following clinical assessments were performed: physical and neurological exam, vital signs (blood pressure, pulse rate, respiratory rate, temperature), weight, clinical laboratory testing (hematology/chemistry), 12-lead electrocardiogram, urine pregnancy test (women of childbearing potential only), review of subject's concomitant medications and assess/record adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	Bulgaria: 26
Country: Number of subjects enrolled	United States: 43
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	Croatia: 6
Country: Number of subjects enrolled	Russian Federation: 64
Worldwide total number of subjects	214
EEA total number of subjects	75

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)	0
Adults (18-64 years)	213
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed the Phase 3, randomized, double-blind, placebo-control trial (804P301) and met the inclusion/exclusion criteria for this trial (804P302) were eligible to participate in this open-label extension safety trial.

Pre-assignment

Screening details:

Subjects who completed the Phase 3, randomized, double-blind, placebo-control trial (804P301) and met the inclusion/exclusion criteria for this trial (804P302) were eligible to participate in this open-label extension safety trial.

Period 1

Period 1 title	Open-Label Extension (OLE) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Intervention Model: Single Group Assignment; Masking: None (Open Label)

Arms

Arm title	Oxcarbazepine extended-release (OXC XR)

Arm description:

Subjects who received at least one dose of Oxcarbazepine extended-release (OXC XR) and had at least 3 weeks of seizure diary data between Week 4 and Week 48 of treatment

Arm type	Open-Label
Investigational medicinal product name	Oxcarbazepine extended-release (OXC XR)
Investigational medicinal product code	
Other name	SPN-804
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oxcarbazepine extended-release (OXC XR) was supplied in 300mg and 600mg tablets. For the first 4 weeks (Day 1 to Day 28) of treatment, subjects took 1200mg OXC XR (two 600mg OXC XR tablets) once daily. From Week 5 to Week 48 (Day 29 to Day 337), the total daily dose of OXC XR could be titrated up or tapered down in increments/decrements of 300mg or 600mg every 3 days between a minimum total daily dose of 600mg/day and maximum total daily dose of 2400mg/day. From Week 49 to Week 52 (Day 338 to 365), subject's total daily dose of OXC XR was then tapered down in decrements of 600mg/day per week until subject is tapered off OXC XR. In addition, during the 52 weeks (12 months) of treatment, subjects continued their adjunctive anti-epileptic drug (AED) treatment(s) (one to three AEDs).

Number of subjects in period 1	Oxcarbazepine extended-release (OXC XR)
Started	214
Completed	179
Not completed	35
Consent withdrawn by subject	9
Physician decision	5

Adverse event, non-fatal	10
Alternative treatment required	2
Non-compliance	2
other	2
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	Open-Label Extension (OLE)
Reporting group description:	
Subjects who received at least one dose of Oxcarbazepine extended-release (OXC XR)	

Reporting group values	Open-Label Extension (OLE)	Total	
Number of subjects	214	214	
Age categorical Units: Subjects			
Adults (18-64 years)	213	213	
Adults (65-84 years)	1	1	
Age continuous Units: years			
arithmetic mean	37.4		
standard deviation	± 11.54	-	
Gender categorical Units: Subjects			
Female	111	111	
Male	103	103	

End points

End points reporting groups

Reporting group title	Oxcarbazepine extended-release (OXC XR)

Reporting group description:

Subjects who received at least one dose of Oxcarbazepine extended-release (OXC XR) and had at least 3 weeks of seizure diary data between Week 4 and Week 48 of treatment

Primary: Percent Seizure Change in Monthly (28-Day) Seizure Frequency (PCH)

End point title	Percent Seizure Change in Monthly (28-Day) Seizure Frequency (PCH)[1]

End point description:

Efficacy was measured as median percent change from baseline monthly 28-day seizure frequency (PCH) to the End of Treatment (EOT, Visit 5, start of OXC XR taper)

End point type	Primary

End point timeframe:

Treatment Period Visits 1-5, Days 0-337

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: There are no statistical data to report other than descriptive statistics (median, minimum and maximum percent change). Since this is an open-label extension trial, there is only one arm. Therefore, no group comparisons are possible. In addition, no statistical comparison(s) between treatment period and baseline were prespecified.

End point values	Oxcarbazepine extended-release (OXC XR)			
Subject group type	Reporting group			
Number of subjects analysed	192			
Units: percent				
median (full range (min-max))	-26.25 (-100.0 to 344.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months of open-label extension trial

Adverse event reporting additional description:

Number of subjects is based on the Safety Population (defined as subjects who took at least one dose of study medication).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Oxcarbazepine extended-release (OXC XR)

Reporting group description:

The number of subjects reported in each treatment arm for serious adverse events and non-serious adverse events is based on the Safety Population, defined as all enrolled subjects who took at least one dose of Oxcarbazepine extended-release (OXC XR).

Serious adverse events	Oxcarbazepine extended-release (OXC XR)		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 214 (7.01%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Prostatic Specific Antigen Increased			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Spinal Fracture			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Transient Ischaemic Attack				
subjects affected / exposed	1 / 214 (0.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 214 (0.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	1 / 214 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Grand Mal Convulsion				
subjects affected / exposed	2 / 214 (0.93%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	2 / 214 (0.93%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	1 / 214 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Hypothermia				
subjects affected / exposed	1 / 214 (0.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Non-Cardiac Chest Pain				
subjects affected / exposed	2 / 214 (0.93%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Psychiatric disorders			
Suicidal Behaviour			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pyelonephritis Acute			
subjects affected / exposed	1 / 214 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Oxcarbazepine extended-release (OXC XR)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 214 (57.94%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	33 / 214 (15.42%)		
occurrences (all)	50		
Headache			
subjects affected / exposed	24 / 214 (11.21%)		
occurrences (all)	29		
Somnolence			
subjects affected / exposed	12 / 214 (5.61%)		
occurrences (all)	15		
Balance Disorder			
subjects affected / exposed	10 / 214 (4.67%)		
occurrences (all)	17		
Eye disorders			

Diplopia subjects affected / exposed occurrences (all)	20 / 214 (9.35%) 26		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	16 / 214 (7.48%) 16 13 / 214 (6.07%) 23		
Respiratory, thoracic and mediastinal disorders Upper respiratory tract infection subjects affected / exposed occurrences (all)	10 / 214 (4.67%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported