Clinical trial results:
A Two-Part Study of ZX008 in Children and Adults with Lennox-Gastaut Syndrome (LGS); Part 1: A Randomized, Double-blind, Placebo-controlled Trial of Two Fixed Doses of ZX008 (Fenfluramine Hydrochloride) Oral Solution as Adjunctive Therapy for Seizures in Children and Adults with LGS, Followed by Part 2: An Open-label Extension to Assess Long-Term Safety of ZX008 in Children and Adults with LGS

Summary

EudraCT number	2017-002628-26
Trial protocol	BE DE ES AT DK GB IT SE NL FR PL
Global end of trial date	23 May 2024

Results information

Result version number	v1
This version publication date	05 January 2025
First version publication date	05 January 2025

Trial information

Trial identification

Sponsor protocol code	ZX008-1601

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03355209
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zogenix International Limited A wholly owned subsidiary of UCB Biosciences, Inc.
Sponsor organisation address	4000 Paramount Pkwy, Suite 200, Morrisville, United States, NC 27560
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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	25 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 May 2024
Global end of trial reached?	Yes
Global end of trial date	23 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Part 1 is the primary objective of the entire study.
The primary objective of Part 1 is: To evaluate the effect of ZX008 0.8 mg/kg/day versus placebo as adjunctive therapy for the treatment of uncontrolled seizures in children and adults with Lennox-Gastaut syndrome (LGS) based on the change in frequency of seizures that result in drops between baseline and the combined Titration and Maintenance Periods (T+M)
The primary objective of Part 2 is to assess the long-term safety and tolerability of ZX008 in children and adults with LGS with regard to AEs, laboratory parameters, physical examination, neurological examination, Tanner Staging, cognition (BRIEF), vital signs (blood pressure, heart rate (HR), temperature, and respiratory rate), electrocardiograms (ECG), echocardiograms (ECHO), body weight, and body mass index (BMI).

Protection of trial subjects:

During the conduct of the study all participants were closely monitored

Background therapy:

Background therapy as permitted in the protocol

Evidence for comparator:

Not applicable

Actual start date of recruitment	27 November 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	72 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Denmark: 3

Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Japan: 33
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	United States: 122
Worldwide total number of subjects	296
EEA total number of subjects	122

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)	117
Adolescents (12-17 years)	87
Adults (18-64 years)	92
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in November 2017 and concluded in May 2024. Cohort A included participants enrolled at sites in North America, Europe, and Australia. Cohort B included participants enrolled at sites in Japan only.

Pre-assignment

Screening details:

The Participant Flow refers to the All Enrolled Participants Set for Part 1 and OLE Safety Population for Part 2 of the study. As planned, Part 2 summaries were presented by the participant's Part 1 treatment groups (placebo, ZX008 0.2 mg/kg/day, ZX008 0.8 mg/kg/day).

Period 1

Period 1 title	Part 1: Double-Blind 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	Cohort A: Placebo

Arm description:

Part 1: Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo at pre-specified time-points.

Arm title	Cohort A: ZX008 0.2 mg/kg/day

Arm description:

Part 1: Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort A: ZX008 0.8 mg/kg/day

Arm description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort B: Placebo

Arm description:

Part 1: Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo at pre-specified time-points.

Arm title	Cohort B: ZX008 0.2 mg/kg/day

Arm description:

Part 1: Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort B: ZX008 0.8 mg/kg/day

Arm description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12
weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Number of subjects in period 1	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day
Started	87	89	87
Completed	86	83	81
Not completed	1	6	6
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	1	1	1
Physician decision	-	1	-
Adverse event, non-fatal	-	4	4

Number of subjects in period 1	Cohort B: Placebo	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day
Started	11	11	11
Completed	11	10	11
Not completed	0	1	0
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	1	-

Period 2

Period 2 title	Part 2:Open-Label Extension (OLE) Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Placebo

Arm description:

Part 1: Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Placebo
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort A: ZX008 0.2 mg/kg/day

Arm description:

Part 1: Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort A: ZX008 0.8 mg/kg/day

Arm description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Arm type	Experimental

Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort B: Placebo

Arm description:

Part 1: Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Placebo
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort B: ZX008 0.2 mg/kg/day

Arm description:

Part 1: Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Arm title	Cohort B: ZX008 0.8 mg/kg/day

Arm description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Arm type	Experimental

Investigational medicinal product name	Fenfluramine hydrochloride
Investigational medicinal product code	ZX008
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received ZX008 at pre-specified time-points.

Number of subjects in period 2[1]	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day
Started	86	83	78
Completed	61	51	46
Not completed	25	32	32
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	6	5	4
Physician decision	-	-	-
Rollover into ZX008-1900	1	-	2
Switching to commercial ZX008	-	-	-
Adverse event, non-fatal	5	5	3
Lack of efficacy	13	21	23

Number of subjects in period 2[1]	Cohort B: Placebo	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day
Started	11	10	11
Completed	5	1	5
Not completed	6	9	6
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	2	-
Physician decision	1	-	1
Rollover into ZX008-1900	-	-	-
Switching to commercial ZX008	5	6	3
Adverse event, non-fatal	-	1	1
Lack of efficacy	-	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 3 participants completed Part 1 but did not receive Part 2 study treatment. Reason for withdrawal after completing Part 1 but not Entering Part 2 was AE/AE/Withdrawal by Subject.

Reporting groups

Reporting group title	Cohort A: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort B: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12

Reporting group values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day
Number of subjects	87	89	87
Age Categorical Units: participants			
2 - < 12 years	32	41	37
12 - < 18 years	29	23	25
18 - 35 years	26	25	25
Age Continuous Units: years			
arithmetic mean	14.4	13.4	13.4
standard deviation	± 7.71	± 7.79	± 7.28
Sex: Female, Male Units: participants			
Female	41	43	33
Male	46	46	54

Reporting group values	Cohort B: Placebo	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day
Number of subjects	11	11	11
Age Categorical Units: participants			
2 - < 12 years	2	3	2
12 - < 18 years	5	2	3
18 - 35 years	4	6	6
Age Continuous Units: years			
arithmetic mean	18.5	20.1	18.5
standard deviation	± 7.78	± 7.79	± 7.94
Sex: Female, Male Units: participants			
Female	5	2	2
Male	6	9	9

Reporting group values	Total		
Number of subjects	296		
Age Categorical Units: participants			
2 - < 12 years	117		
12 - < 18 years	87		
18 - 35 years	92		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	126		

Male	170		

End points reporting groups

Reporting group title	Cohort A: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort B: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12

months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort A: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort A: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Cohort B: Placebo

Reporting group description:

Part 1: Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.2 mg/kg/day

Reporting group description:

Part 1: Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Cohort B: ZX008 0.8 mg/kg/day

Reporting group description:

Part 1: Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days. In Part 2 (OLE Period): Participants initially received ZX008 0.2 mg/kg/day for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Subject analysis set title	Part 2: Cohort A- Overall
Subject analysis set type	Safety analysis

Subject analysis set description:

All Cohort A participants who continued in Part 2 received ZX008 0.2 milligram per kilogram per day (mg/kg/day) as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period.

Subject analysis set title	Part 2: Cohort B- Overall
Subject analysis set type	Safety analysis

Subject analysis set description:

All Cohort B participants who continued in Part 2 received ZX008 0.2 mg/kg/day as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Subject analysis set title	Part 2: Cohort A- Overall
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All Cohort A participants who continued in Part 2 received ZX008 0.2 milligram per kilogram per day (mg/kg/day) as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period.

Subject analysis set title	Part 2: Cohort B- Overall
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All Cohort B participants who continued in Part 2 received ZX008 0.2 mg/kg/day as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Subject analysis set title	Part 2: Cohort A- Overall
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All Cohort A participants who continued in Part 2 received ZX008 0.2 milligram per kilogram per day (mg/kg/day) as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period.

Subject analysis set title	Part 2: Cohort A- Overall
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All Cohort A participants who continued in Part 2 received ZX008 0.2 milligram per kilogram per day (mg/kg/day) as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period.

Subject analysis set title	Part 2: Cohort B- Overall
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All Cohort B participants who continued in Part 2 received ZX008 0.2 mg/kg/day as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Primary: Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC-confirmed) in the combined Titration and Maintenance Period (T+M) in the ZX008 0.8 mg/kg/day group compared to the placebo group

End point title	Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC-confirmed) in the combined Titration and Maintenance Period (T+M) in the ZX008 0.8 mg/kg/day group compared to the placebo group[1]

End point description:

Percent change in frequency of seizures that result in drops (DSF: drop seizure frequency) per 28 days between the combined Titration and Maintenance (T+M) and Baseline. The percent change from Baseline DSF was calculated as the change in DSF between T+M and Baseline / DSF during Baseline* 100. The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. The Modified Intent-to-Treat (mITT) Population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Primary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The 'Cohort A: ZX008 0.2 mg/kg/day' and 'Cohort B: ZX008 0.2 mg/kg/day' arms which was part of baseline period were not required for the primary endpoint assessment. Therefore, no data was reported for this arm.

End point values	Cohort A: Placebo	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo	Cohort B: ZX008 0.8 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	87	11	11
Units: percent change				
median (full range (min-max))	-7.59 (-100.0 to 557.1)	-26.49 (-95.2 to 402.1)	-17.89 (-97.3 to 61.8)	-34.52 (-69.4 to 45.5)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.8 mg/kg/day
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0008
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median Difference (A-P)
Point estimate	-19.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.02
upper limit	-8.74

Notes:

[2] - Median Difference was calculated using Hodges-Lehmann (HL) method.

Primary: Part 2: Percentage of participants with treatment-emergent adverse events (TEAEs)

End point title	Part 2: Percentage of participants with treatment-emergent adverse events (TEAEs)[3]

End point description:

An Adverse event (AE) was defined as any unfavourable and unintended sign, symptom, or disease temporally associated with the use of investigational product, or whether considered related to the investigational product. A TEAE in Part 2 was defined as any AE with an onset on or after the first dose in Part 2. AEs with onset in Part 1 that are ongoing in Part 2 were not included in the count of AEs in Part 2. The OLE Safety Population included all participants who received at least 1 dose of ZX008 during the OLE.

End point type	Primary

End point timeframe:

From Part 2 Baseline until end of the OLE Period (up to 72 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Part 2: Cohort A- Overall	Part 2: Cohort B- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	247	32		
Units: percentage of participants				
number (not applicable)	83.0	96.9		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Percentage of participants with Serious TEAEs

End point title	Part 2: Percentage of participants with Serious TEAEs[4]

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that at any dose: Results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is medically significant. The OLE Safety Population included all participants who received at least 1 dose of ZX008 during the OLE.

End point type	Primary

End point timeframe:

From Part 2 Baseline until end of the OLE Period (up to 72 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Part 2: Cohort A- Overall	Part 2: Cohort B- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	247	32		
Units: percentage of participants				
number (not applicable)	16.6	18.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC-confirmed) in T+M in the ZX008 0.2 mg/kg/day group compared to the placebo group

End point title	Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC-confirmed) in T+M in the ZX008 0.2 mg/kg/day group compared to the placebo group[5]

End point description:

Percent change in frequency of seizures that result in drops (DSF: drop seizure frequency) per 28 days between the combined Titration and Maintenance (T+M) and Baseline. The percent change from Baseline DSF was calculated as the change in DSF between T+M and Baseline / DSF during Baseline* 100. The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for the 'Cohort A: ZX008 0.8 mg/kg/day' and 'Cohort B: ZX008 0.8 mg/kg/day' arms was reported in primary endpoint therefore, these arms which was part of baseline period were not required for the secondary endpoint assessment. Hence, no data was reported for these arms.

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort B: Placebo	Cohort B: ZX008 0.2 mg/kg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	11	11
Units: percent change				
median (full range (min-max))	-7.59 (-100.0 to 557.1)	-14.16 (-100.0 to 3307.3)	-17.89 (-97.3 to 61.8)	-14.12 (-95.6 to 66.4)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.2 mg/kg/day
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.146
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median Difference (A-P)
Point estimate	-10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.99
upper limit	3.99

Notes:

[6] - Median Difference was calculated using HL method.

Secondary: Part 1: Percentage of participants who achieve a >=50% reduction from Baseline in the frequency of seizures that result in drops comparing the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percentage of participants who achieve a >=50% reduction from Baseline in the frequency of seizures that result in drops comparing the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. Participants who achieved a >=50% reduction from Baseline in the DSF, ie, a decrease in DSF of at least 50 percentage points per 28 days during Titration and Maintenance Period. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)	10.3	28.1	25.3	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)	36.4	36.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.8 mg/kg/day
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	6.7

Statistical analysis title	Statistical Analysis 1
Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.2 mg/kg/day
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	7.59

Secondary: Part 1: Percentage of participants who achieve improvement (minimally, much or very much improved) in the CGI-I scale as assessed by Principal Investigator comparing ZX008 0.8 and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percentage of participants who achieve improvement (minimally, much or very much improved) in the CGI-I scale as assessed by Principal Investigator comparing ZX008 0.8 and 0.2 mg/kg/day groups independently versus placebo

End point description:

Clinical Global Impression – Improvement (CGI-I) scale measures improvement in the participant's condition from Baseline. The severity of a participant's condition was rated on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), as follows: 1-very much improved,2-much improved, 3-minimally improved, 4- no change, 5-minimally worse, 6-much worse and 7-very much worse. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

At Day 99 (Visit 12)

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	85	80	11
Units: percentage of participants				
number (not applicable)	33.8	44.7	48.8	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)	45.5	72.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Visit 12

Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.8 mg/kg/day
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0567
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	3.52

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Visit 12	
Comparison groups	Cohort A: Placebo v Cohort A: ZX008 0.2 mg/kg/day
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1565
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.97

Secondary: Part 1: Percent change from Baseline in frequency of all seizures that typically result in drops in T+M, whether ESC-confirmed as drop or not in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in frequency of all seizures that typically result in drops in T+M, whether ESC-confirmed as drop or not in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Seizures that typically result in drops included all: generalized tonic-clonic seizures [GTC], secondarily generalized tonic-clonic [SGTC], tonic seizures [TS], atonic seizures [AS], and tonic/atonic seizures [TA], whether confirmed by the ESC or not. Seizures that result in a drop were defined as seizures involving the entire body, trunk, or head that led to a fall, injury, slumping in a chair, or the participant's head hitting a surface or that could have led to a fall or injury, depending on the patient's position at the time of the seizure. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percent change				
median (full range (min-max))	-8.43 (-100.0 to 557.1)	-11.75 (-100.0 to 3307.3)	-26.28 (-95.2 to 402.1)	-17.89 (-97.3 to 61.8)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-14.12 (-95.6 to 66.4)	-34.04 (-69.4 to 45.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of all countable motor seizures in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in the frequency of all countable motor seizures in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, clonic seizures [CS], hemiclonic seizures [HS], and focal seizures [FS] with clearly observable signs. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percent change				
median (full range (min-max))	-8.43 (-80.8 to 497.8)	-11.75 (-100.0 to 3307.3)	-26.28 (-91.9 to 402.1)	-17.89 (-97.3 to 61.8)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-14.12 (-95.6 to 174.1)	-34.04 (-69.4 to 45.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change from Baseline in the frequency of all countable non-motor seizures in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Change from Baseline in the frequency of all countable non-motor seizures in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable non-motor seizures included: focal seizures [FS] without clear observable signs, myoclonic seizures [MS], absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. For each participant, the seizure frequency per 28 days was calculated as the number of seizures recorded during the period, divided by the number of days in the period and multiplied by 28. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: seizure frequency per 28 days				
median (full range (min-max))	0.00 (-338.3 to 364.3)	0.00 (-418.7 to 675.8)	0.00 (-364.0 to 2952.7)	-7.16 (-30.3 to 13.1)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: seizure frequency per 28 days				
median (full range (min-max))	0.00 (-32.3 to 104.8)	0.00 (-61.6 to 209.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of all countable seizures (motor and non-motor) in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in the frequency of all countable seizures (motor and non-motor) in T+M in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, CS, HS, and FS with clearly observable signs. Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percent change				
median (full range (min-max))	-9.40 (-85.4 to 497.8)	-23.55 (-100.0 to 882.1)	-21.70 (-91.9 to 224.9)	-17.69 (-97.2 to 61.8)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-20.41 (-87.1 to 826.2)	-13.85 (-64.9 to 63.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of seizures that typically result in drops in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in the frequency of seizures that typically result in drops in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Seizures that typically result in drops included all: GTC, SGTC, TS, AS, and TA, whether confirmed by the ESC or not. The mITT Population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	88	86	11
Units: percent change				
median (full range (min-max))	-9.37 (-100.0 to 516.7)	-17.30 (-100.0 to 964.0)	-26.30 (-100.0 to 643.3)	-18.18 (-99.4 to 66.7)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-12.88 (-100.0 to 239.4)	-46.88 (-77.8 to 52.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC confirmed) between Baseline and the Maintenance Period

End point title	Part 1: Percent change from Baseline in the frequency of seizures that result in drops (ESC confirmed) between Baseline and the Maintenance Period

End point description:

The frequency of drop seizures during a given interval was derived from the number and type of events recorded in participant electronic diaries. The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	88	86	11
Units: percent change				
median (full range (min-max))	-7.28 (-100.0 to 516.7)	-18.63 (-100.0 to 964.0)	-27.16 (-100.0 to 643.3)	-18.18 (-99.4 to 66.7)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-12.88 (-100.0 to 239.4)	-45.07 (-77.8 to 52.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of all countable motor seizures in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in the frequency of all countable motor seizures in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable motor seizures included: GTC, SGTC,TS, AS, TA, CS, HS, and FS with clearly observable signs. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	88	86	11
Units: percent change				
median (full range (min-max))	-10.21 (-81.1 to 439.8)	-17.30 (-100.0 to 964.0)	-28.33 (-100.0 to 643.3)	-18.18 (-99.4 to 66.7)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				
median (full range (min-max))	-12.88 (-100.0 to 472.7)	-46.88 (-77.8 to 52.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change from Baseline in the frequency of all countable non-motor seizures in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Change from Baseline in the frequency of all countable non-motor seizures in the Maintenance Period in the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable non-motor seizures included: focal seizures [FS] without clear observable signs, myoclonic seizures [MS], absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. For each participant, the seizure frequency per 28 days was calculated as the number of seizures recorded during the period, divided by the number of days in the period and multiplied by 28. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	88	86	11
Units: seizure frequency per 28 days				
median (full range (min-max))	-0.04 (-340.6 to 362.3)	-0.13 (-442.3 to 588.1)	0.00 (-368.3 to 3219.3)	-4.00 (-30.7 to 15.3)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: seizure frequency per 28 days				
median (full range (min-max))	0.00 (-37.2 to 192.0)	0.00 (-86.8 to 250.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in the frequency of all countable seizures (motor and non-motor) in the Maintenance Period in ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Percent change from Baseline in the frequency of all countable seizures (motor and non-motor) in the Maintenance Period in ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, CS, HS, and FS with clearly observable signs. Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	88	86	11
Units: percent change				
median (full range (min-max))	-9.49 (-85.7 to 439.8)	-27.63 (-100.0 to 211.1)	-23.34 (-100.0 to 254.5)	-18.18 (-99.5 to 66.7)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent change				

median (full range (min-max))	-20.33 (-95.7 to 1626.7)	-17.68 (-72.3 to 80.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percent change from Baseline in frequency of countable seizures that do not result in drops (ESC Confirmed)

End point title	Part 1: Percent change from Baseline in frequency of countable seizures that do not result in drops (ESC Confirmed)

End point description:

Non-drop seizures were defined as any countable seizure types that did not meet the criteria of drop seizures, ie, are classified as CS, HC, FS with or without observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, or other; or are seizures of the following classifications that were approved for each subject as non-drop seizure types by the ESC: GTC, SGTC, TS, AS, or TA. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	73	64	8
Units: percent change				
median (full range (min-max))	-26.92 (-100.0 to 5070.3)	-31.32 (-100.0 to 571.8)	-22.68 (-100.0 to 481.3)	-23.38 (-96.9 to 657.1)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	9		
Units: percent change				
median (full range (min-max))	0.27 (-32.3 to 2915.4)	-22.99 (-85.7 to 138.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline (ie <=0% reduction), or >0, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in seizures that result in drops

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline (ie <=0% reduction), or >0, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in seizures that result in drops

End point description:

The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	37.9	34.8	21.8	36.4
> 0% reduction (T+M) (n=87,89,87,11,11,11)	62.1	65.2	78.2	63.6
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	31.0	47.2	51.7	36.4
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	10.3	28.1	25.3	9.1
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	4.6	10.1	8.0	9.1
100% reduction (T+M) (n=87,89,87,11,11,11)	1.1	1.1	0	0
Near Seizure free (T+M) (n=87,89,87,11,11,11)	1.1	2.2	1.1	0
Worsening or No Change (M) (n=87, 88,86,11,11,11)	40.2	35.2	20.9	36.4
> 0% reduction (M) (n=87, 88,86,11,11,11)	59.8	64.8	79.1	63.6
>= 25% reduction (M) (n=87, 88,86,11,11,11)	33.3	46.6	53.5	36.4
>= 50% reduction (M) (n=87, 88,86,11,11,11)	12.6	31.8	31.4	9.1
>= 75% reduction (M) (n=87, 88,86,11,11,11)	3.4	11.4	14.0	9.1

100% reduction (M) (n=87, 88,86,11,11,11)	1.1	3.4	2.3	0
Near Seizure free (M) (n=87, 88,86,11,11,11)	1.1	4.5	2.3	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	27.3	9.1		
> 0% reduction (T+M) (n=87,89,87,11,11,11)	72.7	90.9		
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	36.4	63.6		
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	36.4	36.4		
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	9.1	0		
100% reduction (T+M) (n=87,89,87,11,11,11)	0	0		
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	0		
Worsening or No Change (M) (n=87, 88,86,11,11,11)	27.3	9.1		
> 0% reduction (M) (n=87, 88,86,11,11,11)	72.7	90.9		
>= 25% reduction (M) (n=87, 88,86,11,11,11)	36.4	72.7		
>= 50% reduction (M) (n=87, 88,86,11,11,11)	36.4	36.4		
>= 75% reduction (M) (n=87, 88,86,11,11,11)	9.1	9.1		
100% reduction (M) (n=87, 88,86,11,11,11)	9.1	0		
Near Seizure free (M) (n=87, 88,86,11,11,11)	9.1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in seizures that typically results in drops

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in seizures that typically results in drops

End point description:

Seizures that typically result in drops included all: GTC, SGTC, TS, AS, and TA, whether confirmed by the ESC or not. The participants who experienced a worsening no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	35.6	36.0	20.7	36.4
> 0% reduction (T+M) (n=87,89,87,11,11,11)	64.4	64.0	79.3	63.6
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	31.0	46.1	50.6	36.4
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	9.2	27.0	26.4	9.1
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	3.4	9.0	8.0	9.1
100% reduction (T+M) (n=87,89,87,11,11,11)	1.1	1.1	0	0
Near Seizure free (T+M) (n=87,89,87,11,11,11)	1.1	1.1	1.1	0
Worsening or No Change (M) (n=87,88,86,11,11,11)	37.9	37.5	19.8	36.4
> 0% reduction (M) (n=87,88,86,11,11,11)	62.1	62.5	80.2	63.6
>= 25% reduction (M) (n=87,88,86,11,11,11)	33.3	45.5	52.3	36.4
>= 50% reduction (M) (n=87,88,86,11,11,11)	10.3	30.7	31.4	9.1
>= 75% reduction (M) (n=87,88,86,11,11,11)	2.3	10.2	12.8	9.1
100% reduction (M) (n=87,88,86,11,11,11)	1.1	2.3	2.3	0
Near Seizure free (M) (n=87,88,86,11,11,11)	1.1	2.3	2.3	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	27.3	9.1		
> 0% reduction (T+M) (n=87,89,87,11,11,11)	72.7	90.9		
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	36.4	63.6		
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	36.4	36.4		
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	9.1	0		
100% reduction (T+M) (n=87,89,87,11,11,11)	0	0		
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	0		
Worsening or No Change (M) (n=87,88,86,11,11,11)	27.3	9.1		
> 0% reduction (M) (n=87,88,86,11,11,11)	72.7	90.9		
>= 25% reduction (M) (n=87,88,86,11,11,11)	36.4	72.7		
>= 50% reduction (M) (n=87,88,86,11,11,11)	36.4	36.4		
>= 75% reduction (M) (n=87,88,86,11,11,11)	9.1	9.1		
100% reduction (M) (n=87,88,86,11,11,11)	9.1	0		
Near Seizure free (M) (n=87,88,86,11,11,11)	9.1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable motor seizures

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable motor seizures

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, CS, HS, and FS with clearly observable signs. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	34.5	38.2	20.7	36.4
> 0% reduction (T+M) (n=87,89,87,11,11,11)	65.5	61.8	79.3	63.6
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	33.3	44.9	50.6	36.4
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	9.2	24.7	25.3	9.1
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	2.3	9.0	6.9	9.1
100% reduction (T+M) (n=87,89,87,11,11,11)	0	1.1	0	0
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	1.1	0	0
Worsening or No Change (M) (n=87,88,86,11,11,11)	36.8	38.6	18.6	36.4
> 0% reduction (M) (n=87,88,86,11,11,11)	63.2	61.4	81.4	63.6
>= 25% reduction (M) (n=87,88,86,11,11,11)	34.5	45.5	53.5	36.4
>= 50% reduction (M) (n=87,88,86,11,11,11)	10.3	28.4	26.7	9.1
>= 75% reduction (M) (n=87,88,86,11,11,11)	1.1	11.4	10.5	9.1
100% reduction (M) (n=87,88,86,11,11,11)	0	2.3	1.2	0
Near Seizure free (M) (n=87,88,86,11,11,11)	0	2.3	1.2	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	27.3	9.1		
> 0% reduction (T+M) (n=87,89,87,11,11,11)	72.7	90.9		
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	36.4	63.6		
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	36.4	36.4		

>= 75% reduction (T+M) (n=87,89,87,11,11,11)	9.1	0		
100% reduction (T+M) (n=87,89,87,11,11,11)	0	0		
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	0		
Worsening or No Change (M) (n=87,88,86,11,11,11)	27.3	9.1		
> 0% reduction (M) (n=87,88,86,11,11,11)	72.7	90.9		
>= 25% reduction (M) (n=87,88,86,11,11,11)	36.4	72.7		
>= 50% reduction (M) (n=87,88,86,11,11,11)	36.4	36.4		
>= 75% reduction (M) (n=87,88,86,11,11,11)	9.1	9.1		
100% reduction (M) (n=87,88,86,11,11,11)	9.1	0		
Near Seizure free (M) (n=87,88,86,11,11,11)	9.1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in countable motor seizures that do not result in drops

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in countable motor seizures that do not result in drops

End point description:

Countable motor seizures included: GTC, SGTC; TS, AS, TA, CS, HS, FS with clearly observable signs. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment. 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	73	64	8
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=70,73,64,8,7,9)	35.7	34.2	34.4	25.0
> 0% reduction (T+M) (n=70,73,64,8,7,9)	64.3	65.8	65.6	75.0
>= 25% reduction (T+M) (n=70,73,64,8,7,9)	51.4	53.4	46.9	50.0
>= 50% reduction (T+M) (n=70,73,64,8,7,9)	30.0	43.8	32.8	25.0
>= 75% reduction (T+M) (n=70,73,64,8,7,9)	12.9	26.0	12.5	12.5
100% reduction (T+M) (n=70,73,64,8,7,9)	2.9	5.5	4.7	0
Near Seizure free (T+M) (n=70,73,64,8,7,9)	2.9	9.6	7.8	0
Worsening or No Change (M) (n=70,72,63,8,7,9)	31.4	33.3	34.9	25.0
> 0% reduction (M) (n=70,72,63,8,7,9)	68.6	66.7	65.1	75.0
>= 25% reduction (M) (n=70,72,63,8,7,9)	54.3	56.9	49.2	50.0
>= 50% reduction (M) (n=70,72,63,8,7,9)	31.4	44.4	33.3	25.0
>= 75% reduction (M) (n=70,72,63,8,7,9)	17.1	29.2	17.5	12.5
100% reduction (M) (n=70,72,63,8,7,9)	5.7	9.7	6.3	12.5
Near Seizure free (M) (n=70,72,63,8,7,9)	7.1	13.9	9.5	12.5

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	9		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=70,73,64,8,7,9)	57.1	44.4		
> 0% reduction (T+M) (n=70,73,64,8,7,9)	42.9	55.6		
>= 25% reduction (T+M) (n=70,73,64,8,7,9)	14.3	44.4		
>= 50% reduction (T+M) (n=70,73,64,8,7,9)	0	22.2		
>= 75% reduction (T+M) (n=70,73,64,8,7,9)	0	11.1		
100% reduction (T+M) (n=70,73,64,8,7,9)	0	0		
Near Seizure free (T+M) (n=70,73,64,8,7,9)	0	0		
Worsening or No Change (M) (n=70,72,63,8,7,9)	57.1	44.4		

> 0% reduction (M) (n=70,72,63,8,7,9)	42.9	55.6		
>= 25% reduction (M) (n=70,72,63,8,7,9)	14.3	44.4		
>= 50% reduction (M) (n=70,72,63,8,7,9)	0	22.2		
>= 75% reduction (M) (n=70,72,63,8,7,9)	0	11.1		
100% reduction (M) (n=70,72,63,8,7,9)	0	0		
Near Seizure free (M) (n=70,72,63,8,7,9)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline (ie <= 0% reduction), or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable seizures

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline (ie <= 0% reduction), or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable seizures

End point description:

Countable motor seizures included: GTC, SGTC; TS, AS, TA, CS, HS, and FS with clearly observable signs. Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	36.8	32.6	28.7	27.3
> 0% reduction (T+M) (n=87,89,87,11,11,11)	63.2	67.4	71.3	72.7
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	35.6	48.3	46.0	27.3
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	11.5	22.5	20.7	9.1

>= 75% reduction (T+M) (n=87,89,87,11,11,11)	3.4	6.7	4.6	9.1
100% reduction (T+M) (n=87,89,87,11,11,11)	0	1.1	0	0
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	1.1	0	0
Worsening or No Change (M) (n=87,88,86,11,11,11)	34.5	33.0	27.9	27.3
> 0% reduction (M) (n=87,88,86,11,11,11)	65.5	67.0	72.1	72.7
>= 25% reduction (M) (n=87,88,86,11,11,11)	34.5	51.1	47.7	27.3
>= 50% reduction (M) (n=87,88,86,11,11,11)	13.8	28.4	24.4	9.1
>= 75% reduction (M) (n=87,88,86,11,11,11)	3.4	9.1	7.0	9.1
100% reduction (M) (n=87,88,86,11,11,11)	0	1.1	1.2	0
Near Seizure free (M) (n=87,88,86,11,11,11)	0	1.1	1.2	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=87,89,87,11,11,11)	27.3	36.4		
> 0% reduction (T+M) (n=87,89,87,11,11,11)	72.7	63.6		
>= 25% reduction (T+M) (n=87,89,87,11,11,11)	27.3	45.5		
>= 50% reduction (T+M) (n=87,89,87,11,11,11)	27.3	27.3		
>= 75% reduction (T+M) (n=87,89,87,11,11,11)	9.1	0		
100% reduction (T+M) (n=87,89,87,11,11,11)	0	0		
Near Seizure free (T+M) (n=87,89,87,11,11,11)	0	0		
Worsening or No Change (M) (n=87,88,86,11,11,11)	27.3	27.3		
> 0% reduction (M) (n=87,88,86,11,11,11)	72.7	72.7		
>= 25% reduction (M) (n=87,88,86,11,11,11)	27.3	45.5		
>= 50% reduction (M) (n=87,88,86,11,11,11)	27.3	27.3		
>= 75% reduction (M) (n=87,88,86,11,11,11)	9.1	0		
100% reduction (M) (n=87,88,86,11,11,11)	0	0		
Near Seizure free (M) (n=87,88,86,11,11,11)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable non-motor seizures

End point title	Part 1: Percentage of participants who achieved a worsening from Baseline, or >0%, >=25%, >=50%, >=75%, 100% reduction, and "near seizure freedom" between Baseline and T+M, and Baseline and M, in all countable non-motor seizures

End point description:

Countable non-motor seizures include: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during T+M); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined T+M Period and Maintenance Period were reported. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment. 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	64	57	8
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=63,64,57,8,7,8)	33.3	34.4	36.8	25.0
> 0% reduction (T+M) (n=63,64,57,8,7,8)	66.7	65.6	63.2	75.0
>= 25% reduction (T+M) (n=63,64,57,8,7,8)	52.4	56.3	43.9	50.0
>= 50% reduction (T+M) (n=63,64,57,8,7,8)	30.2	48.4	35.1	25.0
>= 75% reduction (T+M) (n=63,64,57,8,7,8)	14.3	32.8	12.3	12.5
100% reduction (T+M) (n=63,64,57,8,7,8)	3.2	6.3	3.5	0
Near Seizure free (T+M) (n=63,64,57,8,7,8)	3.2	14.1	5.3	0

Worsening or No Change (M) (n=63,63,56,8,7,8)	30.2	30.2	33.9	12.5
> 0% reduction (M) (n=63,63,56,8,7,8)	69.8	69.8	66.1	87.5
>= 25% reduction (M) (n=63,63,56,8,7,8)	54.0	60.3	48.2	50.0
>= 50% reduction (M) (n=63,63,56,8,7,8)	34.9	49.2	33.9	25.0
>= 75% reduction (M) (n=63,63,56,8,7,8)	17.5	31.7	17.9	12.5
100% reduction (M) (n=63,63,56,8,7,8)	6.3	9.5	8.9	12.5
Near Seizure free (M) (n=63,63,56,8,7,8)	7.9	15.9	10.7	12.5

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change (T+M) (n=63,64,57,8,7,8)	57.1	37.5		
> 0% reduction (T+M) (n=63,64,57,8,7,8)	42.9	62.5		
>= 25% reduction (T+M) (n=63,64,57,8,7,8)	14.3	37.5		
>= 50% reduction (T+M) (n=63,64,57,8,7,8)	0	25.0		
>= 75% reduction (T+M) (n=63,64,57,8,7,8)	0	0		
100% reduction (T+M) (n=63,64,57,8,7,8)	0	0		
Near Seizure free (T+M) (n=63,64,57,8,7,8)	0	0		
Worsening or No Change (M) (n=63,63,56,8,7,8)	57.1	37.5		
> 0% reduction (M) (n=63,63,56,8,7,8)	42.9	62.5		
>= 25% reduction (M) (n=63,63,56,8,7,8)	14.3	37.5		
>= 50% reduction (M) (n=63,63,56,8,7,8)	0	37.5		
>= 75% reduction (M) (n=63,63,56,8,7,8)	0	0		
100% reduction (M) (n=63,63,56,8,7,8)	0	0		
Near Seizure free (M) (n=63,63,56,8,7,8)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change from Baseline in number of seizure-free days during T+M and M Period

End point title	Part 1: Change from Baseline in number of seizure-free days during T+M and M Period

End point description:

A day with no seizures leading to a drop was defined as a day for which electronic (e) diary data were available and no drop seizures were reported. The total number of drop seizure–free days was calculated per 28 days for Baseline and for T+M. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, 'n' included those participants who were evaluable for specified category.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]; During Maintenance Period (12 weeks), compared to Baseline

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: seizure free days per 28 days				
median (full range (min-max))				
T+M Period (n=87,89,87,11,11,11)	0.27 (-5.0 to 16.0)	0.00 (-9.0 to 16.8)	0.29 (-6.1 to 20.0)	0.00 (-2.2 to 23.6)
M Period (n=87,88,86,11,11,11)	0.31 (-5.4 to 15.7)	0.00 (-4.1 to 18.2)	0.16 (-7.4 to 21.7)	-0.65 (-2.7 to 24.7)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: seizure free days per 28 days				
median (full range (min-max))				
T+M Period (n=87,89,87,11,11,11)	0.38 (-2.3 to 22.0)	6.65 (-2.4 to 8.5)		
M Period (n=87,88,86,11,11,11)	0.33 (-7.3 to 26.0)	7.72 (-2.3 to 10.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Duration of longest interval (days) between seizures that result in drops comparing the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point title	Part 1: Duration of longest interval (days) between seizures that result in drops comparing the ZX008 0.8 mg/kg/day and 0.2 mg/kg/day groups independently versus placebo

End point description:

The longest interval between seizures leading to drops were obtained from the eDiary entries in Titration

and Maintenance Period. The interval was derived as the maximum value of the number of days between consecutive drop seizures. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available.

End point type	Secondary

End point timeframe:

From Baseline up to 14 weeks [Titration Period (2 weeks) + Maintenance Period (12 weeks)]

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: days				
median (full range (min-max))	5.00 (1.0 to 39.0)	4.00 (1.0 to 97.0)	5.00 (1.0 to 89.0)	4.00 (1.0 to 91.0)

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: days				
median (full range (min-max))	4.00 (1.0 to 32.0)	6.00 (2.0 to 16.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Clinical Global Impression – Improvement as assessed by the Parent/Caregiver

End point title	Part 1: Clinical Global Impression – Improvement as assessed by the Parent/Caregiver

End point description:

CGI-I scale measures improvement in the participant's condition from Baseline. The severity of a participant's condition was rated on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), as follows: 1-very much improved,2-much improved, 3-minimally improved, 4- no change, 5-minimally worse, 6-much worse and 7-very much worse. The mITT population included all randomized participants who received at least 1 dose of ZX008 or placebo and for whom at least 1 week of diary data were available. Here, number of participants analyzed included those participants who were evaluable for the assessment. 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

At Days (D) 15, 43, 71, and 99

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	85	81	11
Units: percentage of participants				
number (not applicable)				
1=Very much improved (D15) (n=85,85,81,11,10,11)	2.4	5.9	9.9	9.1
2=Much improved (D15) (n=85,85,81,11,10,11)	4.7	15.3	21.0	18.2
3=Minimally improved (D15) (n=85,85,81,11,10,11)	31.8	27.1	39.5	9.1
4=No Change (D15) (n=85,85,81,11,10,11)	51.8	42.4	18.5	63.6
5=Minimally worse (D15) (n=85,85,81,11,10,11)	4.7	5.9	7.4	0
6=Much worse (D15) (n=85,85,81,11,10,11)	4.7	3.5	2.5	0
7=Very much worse (D15) (n=85,85,81,11,10,11)	0	0	1.2	0
1=Very much improved (D43) (n=85,82,80,11,9,10)	1.2	7.3	13.8	9.1
2=Much improved (D43) (n=85,82,80,11,9,10)	9.4	19.5	25.0	0
3=Minimally improved (D43) (n=85,82,80,11,9,10)	20.0	18.3	33.8	18.2
4=No Change (D43) (n=85,82,80,11,9,10)	60.0	39.0	17.5	63.6
5=Minimally worse (D43) (n=85,82,80,11,9,10)	5.9	11.0	5.0	9.1
6=Much worse (D43) (n=85,82,80,11,9,10)	2.4	4.9	5.0	0
7=Very much worse (D43) (n=85,82,80,11,9,10)	1.2	0	0	0
1=Very much improved (D71) (n=82,75,75,11,9,9)	2.4	4.0	10.7	9.1
2=Much improved (D71) (n=82,75,75,11,9,9)	6.1	20.0	28.0	0
3=Minimally improved (D71) (n=82,75,75,11,9,9)	24.4	16.0	33.3	18.2
4=No Change (D71) (n=82,75,75,11,9,9)	53.7	48.0	24.0	63.6
5=Minimally worse (D71) (n=82,75,75,11,9,9)	7.3	8.0	1.3	9.1
6=Much worse (D71) (n=82,75,75,11,9,9)	6.1	4.0	2.7	0
7=Very much worse (D71) (n=82,75,75,11,9,9)	0	0	0	0
1=Very much improved (D99) (n=81,85,80,11,11,11)	1.2	8.2	10.0	9.1
2=Much improved (D99) (n=81,85,80,11,11,11)	3.7	18.8	23.8	0
3=Minimally improved (D99) (n=81,85,80,11,11,11)	32.1	16.5	27.5	18.2
4=No Change (D99) (n=81,85,80,11,11,11)	53.1	37.6	27.5	63.6
5=Minimally worse (D99) (n=81,85,80,11,11,11)	7.4	8.2	5.0	0
6=Much worse (D99) (n=81,85,80,11,11,11)	2.5	7.1	5.0	9.1

7=Very much worse (D99) (n=81,85,80,11,11,11)	0	3.5	1.3	0

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)				
1=Very much improved (D15) (n=85,85,81,11,10,11)	10.0	9.1		
2=Much improved (D15) (n=85,85,81,11,10,11)	10.0	18.2		
3=Minimally improved (D15) (n=85,85,81,11,10,11)	30.0	27.3		
4=No Change (D15) (n=85,85,81,11,10,11)	30.0	27.3		
5=Minimally worse (D15) (n=85,85,81,11,10,11)	20.0	18.2		
6=Much worse (D15) (n=85,85,81,11,10,11)	0	0		
7=Very much worse (D15) (n=85,85,81,11,10,11)	0	0		
1=Very much improved (D43) (n=85,82,80,11,9,10)	0	10.0		
2=Much improved (D43) (n=85,82,80,11,9,10)	22.2	40.0		
3=Minimally improved (D43) (n=85,82,80,11,9,10)	44.4	30.0		
4=No Change (D43) (n=85,82,80,11,9,10)	33.3	0		
5=Minimally worse (D43) (n=85,82,80,11,9,10)	0	20.0		
6=Much worse (D43) (n=85,82,80,11,9,10)	0	0		
7=Very much worse (D43) (n=85,82,80,11,9,10)	0	0		
1=Very much improved (D71) (n=82,75,75,11,9,9)	0	0		
2=Much improved (D71) (n=82,75,75,11,9,9)	22.2	11.1		
3=Minimally improved (D71) (n=82,75,75,11,9,9)	22.2	55.6		
4=No Change (D71) (n=82,75,75,11,9,9)	55.6	22.2		
5=Minimally worse (D71) (n=82,75,75,11,9,9)	0	11.1		
6=Much worse (D71) (n=82,75,75,11,9,9)	0	0		
7=Very much worse (D71) (n=82,75,75,11,9,9)	0	0		
1=Very much improved (D99) (n=81,85,80,11,11,11)	0	18.2		
2=Much improved (D99) (n=81,85,80,11,11,11)	18.2	18.2		
3=Minimally improved (D99) (n=81,85,80,11,11,11)	27.3	36.4		

4=No Change (D99) (n=81,85,80,11,11,11)	45.5	27.3		
5=Minimally worse (D99) (n=81,85,80,11,11,11)	9.1	0		
6=Much worse (D99) (n=81,85,80,11,11,11)	0	0		
7=Very much worse (D99) (n=81,85,80,11,11,11)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants with TEAEs

End point title	Part 1: Percentage of participants with TEAEs

End point description:

Adverse events were defined as any unfavorable and unintended sign (including an abnormal, clinically significant laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. A TEAE in Part 1 was defined as any AE that, based on start date information, occurred after the first dose of study drug in Part 1, but not on or after the first dose of study drug in Part 2. The Safety Population included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to 14 weeks + Taper/Transition (2 weeks)

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)	80.5	78.7	89.7	72.7

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)	90.9	63.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of participants with Serious TEAEs

End point title	Part 1: Percentage of participants with Serious TEAEs

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that at any dose: Results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is medically significant. The Safety Population included all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to 14 weeks + Taper/Transition (2 weeks)

End point values	Cohort A: Placebo	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day	Cohort B: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	89	87	11
Units: percentage of participants				
number (not applicable)	4.6	4.5	11.5	9.1

End point values	Cohort B: ZX008 0.2 mg/kg/day	Cohort B: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage of participants				
number (not applicable)	9.1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Minimum observed plasma concentration of fenfluramine and norfenfluramine at steady state determined directly from the concentration-time profile [Cmin] at steady state

End point title	Part 1: Minimum observed plasma concentration of fenfluramine and norfenfluramine at steady state determined directly from the concentration-time profile [Cmin] at steady state[7]

End point description:

Cmin is the minimum plasma concentration determined directly from the concentration-time profile. The PK analysis set included those participants who received at least one dose of ZX008 and at least one plasma concentration measurement in Study ZX008-1601.

End point type	Secondary

End point timeframe:

At Visit 8 (Day 43) of the Maintenance Period: pre-dose, 1, 2, and 4-6 hours post-dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoints were planned to be reported for ZX008 arms only.

End point values	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	80		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Fenfluramine	8.19 (± 75.6)	31.8 (± 60.8)		
Norfenfluramine	8.23 (± 61.3)	26.2 (± 58.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Maximum observed Plasma concentration of fenfluramine and norfenfluramine determined directly from the concentration time profile [Cmax] at steady state

End point title	Part 1: Maximum observed Plasma concentration of fenfluramine and norfenfluramine determined directly from the concentration time profile [Cmax] at steady state[8]

End point description:

Cmax is the maximum plasma concentration determined directly from the concentration time profile. The PK analysis set included those participants who received at least one dose of ZX008 and at least one plasma concentration measurement in Study ZX008-1601.

End point type	Secondary

End point timeframe:

At Visit 8 (Day 43) of the Maintenance Period: pre-dose, 1, 2, and 4-6 hours post-dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoints were planned to be reported for ZX008 arms only.

End point values	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	80		
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Fenfluramine	11.9 (± 56.1)	44.8 (± 47.0)		
Norfenfluramine	9.04 (± 53.4)	28.9 (± 52.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Area under the concentration-time curve of of fenfluramine and norfenfluramine from time zero to time 24 hours [AUC0-24hours] at steady state

End point title	Part 1: Area under the concentration-time curve of of fenfluramine and norfenfluramine from time zero to time 24 hours [AUC0-24hours] at steady state[9]

End point description:

AUC0-24 is the area under the concentration-time curve from time 0 to 24 hours. The PK analysis set included those participants who received at least one dose of ZX008 and at least one plasma concentration measurement in Study ZX008-1601.

End point type	Secondary

End point timeframe:

At Visit 8 (Day 43) of the Maintenance Period: pre-dose, 1, 2, and 4-6 hours post-dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: PK endpoints were planned to be reported for ZX008 arms only.

End point values	Cohort A: ZX008 0.2 mg/kg/day	Cohort A: ZX008 0.8 mg/kg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	80		
Units: nanograms*hour per milliliter (ng*h/mL)				
geometric mean (geometric coefficient of variation)				
Fenfluramine	246 (± 63.0)	933 (± 52.1)		
Norfenfluramine	209 (± 56.3)	667 (± 55.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent change from Baseline in the frequency of seizures that result in drops (ESC Confirmed) in OLE Period

End point title	Part 2: Percent change from Baseline in the frequency of seizures that result in drops (ESC Confirmed) in OLE Period

End point description:

The frequency of drop seizures during a given interval was derived from the number and type of events recorded in subject electronic diaries. The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily generalized tonic-clonic seizures resulting in drops. The Open-Label Extension Modified Intent-To-Treat (mITT) Population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percent change				
median (full range (min-max))	-43.42 (-99.0 to 64.2)	-29.53 (-100.0 to 2625.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent change from Baseline in the frequency all seizures that typically result in drops between Baseline and the OLE Period whether ESC confirmed as drop or not

End point title	Part 2: Percent change from Baseline in the frequency all seizures that typically result in drops between Baseline and the OLE Period whether ESC confirmed as drop or not

End point description:

Seizures that typically result in drops included all: generalized tonic-clonic seizures [GTC], secondarily generalized tonic-clonic [SGTC], tonic seizures [TS], atonic seizures [AS], and tonic/atonic seizures [TA], whether confirmed by the ESC or not. Seizures that result in a drop were defined as seizures involving the entire body, trunk, or head that led to a fall, injury, slumping in a chair, or the participant's head hitting a surface or that could have led to a fall or injury, depending on the patient’s position at the time of the seizure. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percent change				
median (full range (min-max))	-43.78 (-99.0 to 64.2)	-27.94 (-100.0 to 2625.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent change from Baseline in the frequency of all countable

motor seizures in OLE Period	
End point title	Part 2: Percent change from Baseline in the frequency of all countable motor seizures in OLE Period

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, clonic seizures [CS], hemiclonic seizures [HS], and focal seizures [FS] with clearly observable signs. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percent change				
median (full range (min-max))	-41.94 (-99.0 to 64.2)	-28.18 (-100.0 to 2625.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of seizures that result in drops (ESC confirmed)

End point title	Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of seizures that result in drops (ESC confirmed)

End point description:

The seizure types included in the count were: atonic, tonic, tonic/atonic, generalized tonic-clonic, and secondarily gneralized tonic-clonic seizures resulting in drops. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during OLE Period); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during OLE Period was reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change	18.8	31.5		
> 0%	81.3	68.5		
>= 25%	62.5	55.6		
>= 50%	43.8	32.8		
>= 75%	21.9	12.4		
100%	0	1.2		
Near Seizure free	0	1.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in the frequency of all countable non-motor seizures in OLE Period

End point title	Part 2: Change from Baseline in the frequency of all countable non-motor seizures in OLE Period

End point description:

Countable non-motor seizures included: focal seizures [FS] without clear observable signs, myoclonic seizures [MS], absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. For each participant, the seizure frequency per 28 days was calculated as the number of seizures recorded during the period, divided by the number of days in the period and multiplied by 28. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: seizure frequency per 28 days				
median (full range (min-max))	0.00 (-89.4 to 258.9)	0.00 (-4257.2 to 1774.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percent change from Baseline in the frequency of all countable

seizures (ESC confirmed or not) in OLE Period	
End point title	Part 2: Percent change from Baseline in the frequency of all countable seizures (ESC confirmed or not) in OLE Period

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, CS, HS, and FS with clearly observable signs. Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percent change				
median (full range (min-max))	-28.00 (-99.1 to 83.3)	-28.83 (-100.0 to 606.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in the frequency of all countable seizures that did not result in drops (ESC confirmed) in OLE Period	
End point title	Part 2: Change from Baseline in the frequency of all countable seizures that did not result in drops (ESC confirmed) in OLE Period

End point description:

Non-drop seizures were defined as any countable seizure types that did not meet the criteria of drop seizures, ie, are classified as CS, HC, FS with or without observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, or other; or are seizures of the following classifications that were approved for each participant as non-drop seizure types by the ESC: GTC, SGTC, TS, AS, or TA. For each participant, the seizure frequency per 28 days was calculated as the number of seizures recorded during the period, divided by the number of days in the period and multiplied by 28. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: seizure frequency per 28 days				
median (full range (min-max))	0.00 (-89.4 to 258.9)	-0.99 (-4482.2 to 1774.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of seizures that typically result in drops

End point title	Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of seizures that typically result in drops

End point description:

Seizures that typically result in drops included all: GTC, SGTC, TS, AS, and TA, whether confirmed by the ESC or not. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during OLE Period); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during combined OLE Period were reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change	21.9	32.0		
> 0%	78.1	68.0		
>= 25%	65.6	53.1		
>= 50%	43.8	29.9		
>= 75%	21.9	11.2		
100%	0	0.8		
Near Seizure free	0	1.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable motor seizures

End point title	Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable motor seizures

End point description:

Countable motor seizures included: GTC, SGTC, TS, AS, TA, CS, HS, and FS with clearly observable signs. The participants who experienced a worsening or no change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during OLE Period); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during OLE Period was reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change	21.9	29.5		
> 0%	78.1	70.5		
>= 25%	62.5	54.8		
>= 50%	40.6	29.9		
>= 75%	21.9	9.1		
100%	0	0.4		
Near Seizure free	0	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable non-motor seizures

End point title	Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable non-motor seizures

End point description:

Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The participants who experienced a worsening or change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during OLE Period); and "near

seizure freedom," (defined as 0 or 1 seizure leading to a drop) during OLE Period was reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change	37.5	24.1		
> 0%	31.3	46.1		
>= 25%	25.0	41.9		
>= 50%	18.8	34.0		
>= 75%	6.3	22.8		
100%	3.1	4.6		
Near Seizure free	6.3	7.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable seizures

End point title	Part 2: Percentage of participants who achieved a worsening from Baseline, or > 0%, >=25%, >= 50%, >= 75%, 100% reduction, and "near seizure freedom" from Baseline in frequency of all countable seizures

End point description:

Countable motor seizures included: GTC, SGTC; TS, AS, TA, CS, HS, and FS with clearly observable signs. Countable non-motor seizures included: FS without clear observable signs, MS, absence/atypical absence, infantile spasms, epileptic spasms, and other seizures. The participants who experienced a worsening or change from Baseline (ie <= 0% reduction); >0%, >=25%, >=50%, >=75%, and 100% reduction (a 100% reduction was equivalent to achieving seizure freedom during OLE Period); and "near seizure freedom," (defined as 0 or 1 seizure leading to a drop) during OLE Period were reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From OLE Month 1 to Month12, compared to Baseline (Part 1)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: percentage of participants				
number (not applicable)				
Worsening or No Change	37.5	30.3		
> 0%	62.5	69.7		
>= 25%	56.3	53.1		
>= 50%	28.1	30.7		
>= 75%	12.5	9.1		
100%	0	0.4		
Near Seizure free	0	0.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Clinical Global Impression – Improvement as assessed by the Principal Investigator

End point title	Part 2: Clinical Global Impression – Improvement as assessed by the Principal Investigator

End point description:

CGI-I scale measures improvement in the participant's condition from Baseline. The severity of a participant's condition was rated on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), as follows: 1-very much improved,2-much improved, 3-minimally improved, 4- no change, 5-minimally worse, 6-much worse and 7-very much worse. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE. Here, number of participants analyzed included those participants who were evaluable for the assessment. 'n' analyzed included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

At OLE Day 1, OLE Months (M) 1, 2, 3, 6, 9, 12, and Last Assessment (up to 72 months)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	237		
Units: percentage of participants				
number (not applicable)				
1=Very much improved (OLE D1) (n=236,32)	3.1	2.5		
2=Much improved (OLE D1) (n=236,32)	18.8	15.3		
3=Minimally improved (OLE D1) (n=236,32)	18.8	25.8		
4=No Change (OLE D1) (n=236,32)	56.3	48.3		
5=Minimally worse (OLE D1)(n=236,32)	3.1	7.2		
6=Much worse (OLE D1) (n=236,32)	0	0.8		

7=Very much worse (OLE D1) (n=236,32)	0	0		
1=Very much improved (OLE M1) (n=225,32)	9.4	4.4		
2=Much improved (OLE M1) (n=225,32)	21.9	20.0		
3=Minimally improved (OLE M1) (n=225,32)	37.5	32.4		
4=No Change (OLE M1) (n=225,32)	31.3	34.2		
5=Minimally worse (OLE M1) (n=225,32)	0	7.6		
6=Much worse (OLE M1) (n=225,32)	0	1.3		
7=Very much worse (OLE M1) (n=225,32)	0	0		
1=Very much improved (OLE M2) (n=220,31)	6.5	5.5		
2=Much improved (OLE M2) (n=220,31)	19.4	24.5		
3=Minimally improved (OLE M2) (n=220,31)	35.5	34.1		
4=No Change (OLE M2) (n=220,31)	32.3	27.7		
5=Minimally worse (OLE M2) (n=220,31)	6.5	5.0		
6=Much worse (OLE M2) (n=220,31)	0	3.2		
7=Very much worse (OLE M2) (n=220,31)	0	0		
1=Very much improved (OLE M3) (n=207,29)	6.9	7.2		
2=Much improved (OLE M3) (n=207,29)	17.2	25.1		
3=Minimally improved (OLE M3) (n=207,29)	55.2	36.2		
4=No Change (OLE M3) (n=207,29)	20.7	21.7		
5=Minimally worse (OLE M3) (n=207,29)	0	7.2		
6=Much worse (OLE M3) (n=207,29)	0	2.4		
7=Very much worse (OLE M3) (n=207,29)	0	0		
1=Very much improved (OLE M6) (n=184,29)	3.4	8.2		
2=Much improved (OLE M6) (n=184,29)	27.6	33.7		
3=Minimally improved (OLE M6) (n=184,29)	34.5	31.0		
4=No Change (OLE M6) (n=184,29)	27.6	20.1		
5=Minimally worse (OLE M6) (n=184,29)	6.9	3.8		
6=Much worse (OLE M6) (n=184,29)	0	3.3		
7=Very much worse (OLE M6) (n=184,29)	0	0		
1=Very much improved (OLE M9) (n=133,28)	3.6	9.0		
2=Much improved (OLE M9) (n=133,28)	28.6	37.6		
3=Minimally improved (OLE M9) (n=133,28)	28.6	27.1		
4=No Change (OLE M9) (n=133,28)	35.7	18.8		
5=Minimally worse (OLE M9) (n=133,28)	3.6	6.0		
6=Much worse (OLE M9) (n=133,28)	0	1.5		
7=Very much worse (OLE M9) (n=133,28)	0	0		
1=Very much improved (OLE M12) (n=145,26)	0	9.7		

2=Much improved (OLE M12) (n=145,26)	53.8	39.3		
3=Minimally improved (OLE M12) (n=145,26)	23.1	26.2		
4=No Change (OLE M12) (n=145,26)	19.2	18.6		
5=Minimally worse (OLE M12) (n=145,26)	3.8	3.4		
6=Much worse (OLE M12) (n=145,26)	0	2.8		
7=Very much worse (OLE M12) (n=145,26)	0	0		
1=Very much improved (Last Assessment) (n=)	6.3	7.6		
2=Much improved (Last Assessment) (n=237,32)	25.0	27.4		
3=Minimally improved (Last Assessment) (n=237,32)	25.0	21.9		
4=No Change (Last Assessment) (n=237,32)	40.6	28.3		
5=Minimally worse (Last Assessment) (n=237,32)	3.1	7.2		
6=Much worse (Last Assessment) (n=237,32)	0	7.6		
7=Very much worse (Last Assessment) (n=237,32)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in number of seizure-free days per 28 Days (ESC Confirmed) in OLE Period

End point title	Part 2: Change from Baseline in number of seizure-free days per 28 Days (ESC Confirmed) in OLE Period

End point description:

A day with no seizures leading to a drop was defined as a day for which ediary data were available and no drop seizures were reported. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE.

End point type	Secondary

End point timeframe:

From Part 2 Baseline until end of OLE Period (up to 72 months)

End point values	Part 2: Cohort B- Overall	Part 2: Cohort A- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	241		
Units: seizure free days per 28 days				
median (full range (min-max))	4.24 (-3.6 to 24.5)	2.16 (-23.0 to 27.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Baseline in duration of Longest interval between seizures that result in drops (ESC Confirmed) in OLE Period

End point title	Part 2: Change from Baseline in duration of Longest interval between seizures that result in drops (ESC Confirmed) in OLE Period

End point description:

The longest interval between seizures leading to drops were obtained from the eDiary entries in OLE Period. The interval was derived as the maximum value of the number of days between consecutive drop seizures. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE. Here, number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

From Part 2 Baseline until end of the OLE Period (up to 72 months)

End point values	Part 2: Cohort A- Overall	Part 2: Cohort B- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	241	27		
Units: days				
median (full range (min-max))	4.0 (-10 to 360)	6.0 (0 to 200)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Clinical Global Impression – Improvement as assessed by the Parent/Caregiver

End point title	Part 2: Clinical Global Impression – Improvement as assessed by the Parent/Caregiver

End point description:

CGI-I scale measures improvement in the participant's condition from Baseline. The severity of a participant's condition was rated on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse), as follows: 1-very much improved,2-much improved, 3-minimally improved, 4- no change, 5-minimally worse, 6-much worse and 7-very much worse. The OLE mITT population included all participants who received at least 1 dose of ZX008 and had a valid estimate of the frequency of seizures that resulted in drops from Part 1 and at least 1 month (30 days) of valid seizure data during the OLE. Here, number of participants analyzed included those participants who were evaluable for the assessment. 'n' included those participants who were evaluable at specified time point.

End point type	Secondary

End point timeframe:

At OLE Day 1, OLE Months (M) 1, 2, 3, 6, 9, 12, and Last Assessment (up to 72 months)

End point values	Part 2: Cohort A- Overall	Part 2: Cohort B- Overall		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	237	32		
Units: percentage of participants				
number (not applicable)				
1=Very much improved (OLE D1) (n=232,32)	6.9	9.4		
2=Much improved (OLE D1) (n=232,32)	16.8	12.5		
3=Minimally improved (OLE D1) (n=232,32)	24.6	28.1		
4=No Change (OLE D1) (n=232,32)	40.1	43.8		
5=Minimally worse (OLE D1) (n=232,32)	6.9	3.1		
6=Much worse (OLE D1) (n=232,32)	3.9	3.1		
7=Very much worse (OLE D1) (n=232,32)	0.9	0		
1=Very much improved (OLE M1) (n=224,32)	7.1	12.5		
2=Much improved (OLE M1) (n=224,32)	21.4	15.6		
3=Minimally improved (OLE M1) (n=224,32)	32.1	31.3		
4=No Change (OLE M1) (n=224,32)	29.5	40.6		
5=Minimally worse (OLE M1) (n=224,32)	5.8	0		
6=Much worse (OLE M1) (n=224,32)	4.0	0		
7=Very much worse (OLE M1) (n=224,32)	0	0		
1=Very much improved (OLE M2) (n=219,31)	7.3	12.9		
2=Much improved (OLE M2) (n=219,31)	25.6	16.1		
3=Minimally improved (OLE M2) (n=219,31)	32.0	41.9		
4=No Change (OLE M2) (n=219,31)	25.6	22.6		
5=Minimally worse (OLE M2) (n=219,31)	6.4	6.5		
6=Much worse (OLE M2) (n=219,31)	2.3	0		
7=Very much worse (OLE M2) (n=219,31)	0.9	0		
1=Very much improved (OLE M3) (n=207,29)	9.7	13.8		
2=Much improved (OLE M3) (n=207,29)	30.0	10.3		
3=Minimally improved (OLE M3) (n=207,29)	29.5	37.9		
4=No Change (OLE M3) (n=207,29)	19.3	37.9		
5=Minimally worse (OLE M3) (n=207,29)	9.7	0		
6=Much worse (OLE M3) (n=207,29)	0.5	0		
7=Very much worse (OLE M3) (n=207,29)	1.4	0		

1=Very much improved (OLE M6) (n=186,29)	13.4	10.3		
2=Much improved (OLE M6) (n=186,29)	30.1	31.0		
3=Minimally improved (OLE M6) (n=186,29)	27.4	34.5		
4=No Change (OLE M6) (n=186,29)	23.1	20.7		
5=Minimally worse (OLE M6) (n=186,29)	3.2	0		
6=Much worse (OLE M6) (n=186,29)	2.2	3.4		
7=Very much worse (OLE M6) (n=186,29)	0.5	0		
1=Very much improved (OLE M9) (n=134,28)	13.4	14.3		
2=Much improved (OLE M9) (n=134,28)	37.3	25.0		
3=Minimally improved (OLE M9) (n=134,28)	26.1	21.4		
4=No Change (OLE M9) (n=134,28)	14.2	32.1		
5=Minimally worse (OLE M9) (n=134,28)	8.2	3.6		
6=Much worse (OLE M9) (n=134,28)	0.7	3.6		
7=Very much worse (OLE M9) (n=134,28)	0	0		
1=Very much improved (OLE M12) (n=149,26)	16.8	19.2		
2=Much improved (OLE M12) (n=149,26)	34.2	26.9		
3=Minimally improved (OLE M12) (n=149,26)	26.8	46.2		
4=No Change (OLE M12) (n=149,26)	14.8	3.8		
5=Minimally worse (OLE M12) (n=149,26)	4.7	3.8		
6=Much worse (OLE M12) (n=149,26)	2.0	0		
7=Very much worse (OLE M12) (n=149,26)	0.7	0		
1=Very much improved (Last Assessment) (n=237,32)	11.4	12.5		
2=Much improved (Last Assessment) (n=237,32)	24.1	28.1		
3=Minimally improved (Last Assessment) (n=237,32)	24.5	18.8		
4=No Change (Last Assessment) (n=237,32)	25.3	28.1		
5=Minimally worse (Last Assessment) (n=237,32)	9.3	9.4		
6=Much worse (Last Assessment) (n=237,32)	3.4	3.1		
7=Very much worse (Last Assessment) (n=237,32)	2.1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to 72 months

Adverse event reporting additional description:

AEs with onset in Part 1 that are ongoing in Part 2 were not included in the count of AEs in Part 2. Safety Population and OLE Safety Population were assessed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Part 1:Cohort A- Placebo

Reporting group description:

Participants received matching placebo as an oral solution, twice a day (bid) over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Reporting group title	Part 1: Cohort A- ZX008 0.8 mg/kg/day

Reporting group description:

Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant stiripentol [STP]). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Reporting group title	Part 1: Cohort A- ZX008 0.2 mg/kg/day

Reporting group description:

Participants received ZX008 0.2 milligram per kilogram per day (mg/kg/day) during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Reporting group title	Part 2: Cohort A- Overall

Reporting group description:

All Cohort A participants who continued in Part 2 received ZX008 0.2 milligram per kilogram per day (mg/kg/day) as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period.

Reporting group title	Part 1: Cohort B- ZX008 0.8 mg/kg/day

Reporting group description:

Participants were titrated to their blinded randomized dose of ZX008 over the 2-week Titration from 0.2 mg/kg/day to ZX008 0.8 mg/kg/day (or a maximum dose of 30 mg/day or 20 mg/day for participants taking concomitant STP). Following titration, participants continued to receive the randomized dose of ZX008 as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Reporting group title	Part 1: Cohort B- ZX008 0.2 mg/kg/day

Reporting group description:

Participants received ZX008 0.2 mg/kg/day during the 2-week Titration. Following titration, participants received ZX008 0.2 mg/kg/day as an oral solution, bid for an additional 12 weeks during Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Reporting group title	Part 2: Cohort B- Overall

Reporting group description:

All Cohort B participants who continued in Part 2 received ZX008 0.2 mg/kg/day as an oral solution, twice a day (bid), for 1 month. After 1 month at a dose of ZX008 0.2 mg/kg/day, the Investigator could adjust the dose if needed. Dose changes were made in maximum increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day (or 0.5 mg/kg/day for participants taking concomitant STP) but not to exceed a total dose of 30 mg/day (or 20 mg/kg/day for subjects taking concomitant STP). Participants received ZX008 for up to 12 months in OLE Period. Participants who completed 12 months OLE Period had option to receive ZX008 for up to 72 months, or until ZX008 is approved in the participant's country.

Reporting group title	Part 1: Cohort B- Placebo

Reporting group description:

Participants received matching placebo as an oral solution, bid over 2 weeks of Titration Period and an additional 12 weeks of Maintenance Period. Participants who completed the Maintenance Period and did not continue in Part 2, and participants who discontinued from Part 1 early, were tapered off study medication over 8 days.

Serious adverse events	Part 1:Cohort A-Placebo	Part 1: Cohort A-ZX008 0.8 mg/kg/day	Part 1: Cohort A-ZX008 0.2 mg/kg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 87 (4.60%)	10 / 87 (11.49%)	4 / 89 (4.49%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Distributive shock			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden unexplained death in epilepsy			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Asthenia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Pleurisy			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stereotypy			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Hallucination			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Agitation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood prolactin increased			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Foreign body in respiratory tract			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Somnolence			

subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Seizure			
subjects affected / exposed	2 / 87 (2.30%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Change in seizure presentation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	2 / 89 (2.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 87 (1.15%)	3 / 87 (3.45%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure cluster			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye movement disorder			
subjects affected / exposed	1 / 87 (1.15%)	0 / 87 (0.00%)	0 / 89 (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
Keratoconus			

subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Gastritis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Tooth loss			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental caries			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Endocrine disorders			

Thyroid mass			
subjects affected / exposed	1 / 87 (1.15%)	0 / 87 (0.00%)	0 / 89 (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
Infections and infestations			
Infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 87 (0.00%)	2 / 87 (2.30%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter bacteraemia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Cohort A-Overall	Part 1: Cohort B-ZX008 0.8 mg/kg/day	Part 1: Cohort B-ZX008 0.2 mg/kg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 247 (16.60%)	0 / 11 (0.00%)	1 / 11 (9.09%)
number of deaths (all causes)	1	0	0

number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Distributive shock			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
General disorders and administration site conditions			
Sudden unexplained death in epilepsy			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Pyrexia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stereotypy			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Hallucination			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Agitation			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Investigations			
Blood prolactin increased			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Weight decreased			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Humerus fracture			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Foreign body in respiratory tract			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Facial bones fracture			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Somnolence			
subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	2 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Change in seizure presentation			
subjects affected / exposed	10 / 247 (4.05%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	3 / 12	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	8 / 247 (3.24%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 25	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Seizure cluster			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Eye disorders			
Eye movement disorder			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoconus			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth loss			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Dental caries			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 247 (2.02%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Subcutaneous abscess			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Dengue fever			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Urinary tract infection			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Influenza			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Enterobacter bacteraemia			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (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
Decreased appetite			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Cohort B-Overall	Part 1: Cohort B-Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 32 (18.75%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Distributive shock			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden unexplained death in epilepsy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication of device insertion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Stereotypy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood prolactin increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body in respiratory tract			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Foreign body in gastrointestinal tract			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Change in seizure presentation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure cluster			
subjects affected / exposed	2 / 32 (6.25%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eye disorders			
Eye movement disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoconus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth loss			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter bacteraemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			

subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1:Cohort A-Placebo	Part 1: Cohort A-ZX008 0.8 mg/kg/day	Part 1: Cohort A-ZX008 0.2 mg/kg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 87 (68.97%)	68 / 87 (78.16%)	64 / 89 (71.91%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 87 (12.64%)	9 / 87 (10.34%)	11 / 89 (12.36%)
occurrences (all)	13	10	12
Oedema peripheral			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	11 / 87 (12.64%)	16 / 87 (18.39%)	8 / 89 (8.99%)
occurrences (all)	11	18	10
Asthenia			
subjects affected / exposed	3 / 87 (3.45%)	5 / 87 (5.75%)	4 / 89 (4.49%)
occurrences (all)	5	5	4
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	3 / 87 (3.45%)	4 / 87 (4.60%)	2 / 89 (2.25%)
occurrences (all)	3	4	3
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	1 / 89 (1.12%)
occurrences (all)	0	0	1
Irritability			

subjects affected / exposed	5 / 87 (5.75%)	4 / 87 (4.60%)	9 / 89 (10.11%)
occurrences (all)	5	4	9
Insomnia			
subjects affected / exposed	3 / 87 (3.45%)	2 / 87 (2.30%)	0 / 89 (0.00%)
occurrences (all)	3	2	0
Affective disorder			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	3 / 87 (3.45%)	1 / 87 (1.15%)	1 / 89 (1.12%)
occurrences (all)	3	1	2
Investigations			
Echocardiogram abnormal			
subjects affected / exposed	6 / 87 (6.90%)	2 / 87 (2.30%)	2 / 89 (2.25%)
occurrences (all)	6	2	2
Weight decreased			
subjects affected / exposed	2 / 87 (2.30%)	7 / 87 (8.05%)	3 / 89 (3.37%)
occurrences (all)	2	7	3
Blood prolactin increased			
subjects affected / exposed	1 / 87 (1.15%)	3 / 87 (3.45%)	0 / 89 (0.00%)
occurrences (all)	1	4	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 87 (1.15%)	5 / 87 (5.75%)	2 / 89 (2.25%)
occurrences (all)	1	5	3
Face injury			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	1 / 87 (1.15%)	3 / 87 (3.45%)	2 / 89 (2.25%)
occurrences (all)	1	3	2
Hand fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	1 / 89 (1.12%)
occurrences (all)	0	0	1
Ligament sprain			

subjects affected / exposed	2 / 87 (2.30%)	1 / 87 (1.15%)	1 / 89 (1.12%)
occurrences (all)	2	1	1
Lip injury			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	2 / 87 (2.30%)	1 / 87 (1.15%)	1 / 89 (1.12%)
occurrences (all)	2	1	1
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Lethargy			
subjects affected / exposed	3 / 87 (3.45%)	5 / 87 (5.75%)	4 / 89 (4.49%)
occurrences (all)	3	5	4
Change in seizure presentation			
subjects affected / exposed	2 / 87 (2.30%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	2	0	0
Seizure cluster			
subjects affected / exposed	1 / 87 (1.15%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	4 / 87 (4.60%)	5 / 87 (5.75%)	11 / 89 (12.36%)
occurrences (all)	4	6	13
Somnolence			
subjects affected / exposed	10 / 87 (11.49%)	15 / 87 (17.24%)	10 / 89 (11.24%)
occurrences (all)	10	16	11
Tremor			
subjects affected / exposed	1 / 87 (1.15%)	2 / 87 (2.30%)	2 / 89 (2.25%)
occurrences (all)	1	2	2
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	4 / 87 (4.60%)	10 / 87 (11.49%)	10 / 89 (11.24%)
occurrences (all)	4	11	10
Breath odour			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	5 / 87 (5.75%)	8 / 87 (9.20%)	5 / 89 (5.62%)
occurrences (all)	5	10	5
Dental caries			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	2 / 89 (2.25%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	5 / 87 (5.75%)	9 / 87 (10.34%)	11 / 89 (12.36%)
occurrences (all)	5	44	16
Haemorrhoids			
subjects affected / exposed	1 / 87 (1.15%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	2 / 89 (2.25%)
occurrences (all)	0	0	2
Dermatitis diaper			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Miliaria			

subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 87 (0.00%)	3 / 87 (3.45%)	0 / 89 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 87 (0.00%)	2 / 87 (2.30%)	2 / 89 (2.25%)
occurrences (all)	0	2	2
Conjunctivitis			
subjects affected / exposed	0 / 87 (0.00%)	2 / 87 (2.30%)	1 / 89 (1.12%)
occurrences (all)	0	2	1
Corona virus infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	2 / 87 (2.30%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 87 (4.60%)	6 / 87 (6.90%)	7 / 89 (7.87%)
occurrences (all)	4	7	10
Sinusitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	1 / 89 (1.12%)
occurrences (all)	0	1	1
Rhinitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	1 / 89 (1.12%)
occurrences (all)	0	1	2
Oral herpes			

subjects affected / exposed	0 / 87 (0.00%)	1 / 87 (1.15%)	0 / 89 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	8 / 87 (9.20%)	7 / 87 (8.05%)	4 / 89 (4.49%)
occurrences (all)	10	8	5
Influenza			
subjects affected / exposed	1 / 87 (1.15%)	1 / 87 (1.15%)	4 / 89 (4.49%)
occurrences (all)	1	1	4
Herpes zoster			
subjects affected / exposed	0 / 87 (0.00%)	0 / 87 (0.00%)	0 / 89 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 87 (14.94%)	32 / 87 (36.78%)	18 / 89 (20.22%)
occurrences (all)	15	35	18

Non-serious adverse events	Part 2: Cohort A-Overall	Part 1: Cohort B-ZX008 0.8 mg/kg/day	Part 1: Cohort B-ZX008 0.2 mg/kg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	166 / 247 (67.21%)	7 / 11 (63.64%)	10 / 11 (90.91%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	25 / 247 (10.12%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	33	0	0
Oedema peripheral			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	33 / 247 (13.36%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	35	0	0
Asthenia			
subjects affected / exposed	7 / 247 (2.83%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	8	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			

subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	10 / 247 (4.05%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	11	0	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	5 / 247 (2.02%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	5	1	0
Irritability			
subjects affected / exposed	6 / 247 (2.43%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Insomnia			
subjects affected / exposed	11 / 247 (4.45%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	11	0	0
Affective disorder			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	3
Agitation			
subjects affected / exposed	4 / 247 (1.62%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Investigations			
Echocardiogram abnormal			
subjects affected / exposed	6 / 247 (2.43%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Weight decreased			
subjects affected / exposed	12 / 247 (4.86%)	4 / 11 (36.36%)	2 / 11 (18.18%)
occurrences (all)	12	4	2
Blood prolactin increased			
subjects affected / exposed	9 / 247 (3.64%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	10	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	7 / 247 (2.83%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	10	0	0
Face injury			

subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Laceration			
subjects affected / exposed	13 / 247 (5.26%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	13	0	0
Hand fracture			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Ligament sprain			
subjects affected / exposed	4 / 247 (1.62%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Lip injury			
subjects affected / exposed	6 / 247 (2.43%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Wound			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nervous system disorders			
Lethargy			
subjects affected / exposed	13 / 247 (5.26%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	13	0	0
Change in seizure presentation			
subjects affected / exposed	17 / 247 (6.88%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	19	0	0
Seizure cluster			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	24 / 247 (9.72%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	28	0	0
Somnolence			

subjects affected / exposed	24 / 247 (9.72%)	3 / 11 (27.27%)	4 / 11 (36.36%)
occurrences (all)	26	3	5
Tremor			
subjects affected / exposed	7 / 247 (2.83%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	7	1	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	13 / 247 (5.26%)	2 / 11 (18.18%)	3 / 11 (27.27%)
occurrences (all)	15	2	3
Breath odour			
subjects affected / exposed	0 / 247 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	18 / 247 (7.29%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	22	0	0
Dental caries			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	13 / 247 (5.26%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	17	0	0
Haemorrhoids			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	1 / 247 (0.40%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Acne			
subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Eczema			

subjects affected / exposed	2 / 247 (0.81%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Dermatitis diaper			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dermatitis atopic			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	3 / 247 (1.21%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	4	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Corona virus infection			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	2 / 247 (0.81%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Upper respiratory tract infection			

subjects affected / exposed	16 / 247 (6.48%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	20	1	0
Sinusitis			
subjects affected / exposed	5 / 247 (2.02%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Rhinitis			
subjects affected / exposed	5 / 247 (2.02%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Oral herpes			
subjects affected / exposed	0 / 247 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	31 / 247 (12.55%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	43	0	2
Influenza			
subjects affected / exposed	3 / 247 (1.21%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Herpes zoster			
subjects affected / exposed	1 / 247 (0.40%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	39 / 247 (15.79%)	3 / 11 (27.27%)	3 / 11 (27.27%)
occurrences (all)	42	3	4

Non-serious adverse events	Part 2: Cohort B-Overall	Part 1: Cohort B-Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 32 (93.75%)	8 / 11 (72.73%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 32 (21.88%)	1 / 11 (9.09%)	
occurrences (all)	12	1	
Oedema peripheral			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Fatigue			

subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	3 / 32 (9.38%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Cough			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Irritability			
subjects affected / exposed	3 / 32 (9.38%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Insomnia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Affective disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Investigations			
Echocardiogram abnormal			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Weight decreased			
subjects affected / exposed	4 / 32 (12.50%)	1 / 11 (9.09%)	
occurrences (all)	4	1	
Blood prolactin increased			

subjects affected / exposed	8 / 32 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	14	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 32 (9.38%)	1 / 11 (9.09%)	
occurrences (all)	5	1	
Face injury			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Hand fracture			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Lip injury			
subjects affected / exposed	3 / 32 (9.38%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Wound			
subjects affected / exposed	4 / 32 (12.50%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Lethargy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Change in seizure presentation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Seizure cluster			

subjects affected / exposed	2 / 32 (6.25%)	1 / 11 (9.09%)	
occurrences (all)	5	2	
Seizure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	11 / 32 (34.38%)	1 / 11 (9.09%)	
occurrences (all)	16	1	
Tremor			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Diplopia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 32 (15.63%)	0 / 11 (0.00%)	
occurrences (all)	5	0	
Breath odour			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	5 / 32 (15.63%)	0 / 11 (0.00%)	
occurrences (all)	7	0	
Dental caries			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			

Alopecia areata			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Acne			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	5 / 32 (15.63%)	0 / 11 (0.00%)	
occurrences (all)	7	0	
Dermatitis diaper			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Dermatitis atopic			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Miliaria			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 32 (9.38%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Corona virus infection			
subjects affected / exposed	12 / 32 (37.50%)	0 / 11 (0.00%)	
occurrences (all)	14	0	
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gastroenteritis			

subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 32 (0.00%)	0 / 11 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	9 / 32 (28.13%)	2 / 11 (18.18%)	
occurrences (all)	18	2	
Influenza			
subjects affected / exposed	3 / 32 (9.38%)	1 / 11 (9.09%)	
occurrences (all)	3	1	
Herpes zoster			
subjects affected / exposed	2 / 32 (6.25%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 32 (12.50%)	2 / 11 (18.18%)	
occurrences (all)	4	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2018	Amendment 1.0 provided updates and clarifications on the cardiac follow-up windows, added MS that result in a drop to the types of seizures assessed in the secondary endpoints, clarified inclusion and exclusion criteria, and clarified information to be recorded for adverse event reporting.
29 July 2019	Amendment 2.1 combined details from all country-specific protocols into 1 global document, incorporated corrections of the maximum daily dose for subjects taking concomitant STP, updated background information about completed and ongoing clinical trials, and provided updated information about the following: ECHO alert levels for trace regurgitation, endpoints and objectives, statistical analyses, increases in enrollment numbers, visit window allowances during the transition between Part 1 and Part 2, options for continuation of treatment after the end of the trial, prohibited medications, acceptable collection methods for urinalysis samples, phone visit options for Visit 13 and 23, and parameters regarding repeat laboratory sample collection during Baseline. It also included corrections to blood collection volumes and edits for consistency throughout.
02 July 2020	Amendment 3.1 provided study conduct information for the COVID-19 pandemic. This amendment also removed the Vineland Adaptive Behavior Scale (VABS) from the study assessments, included updated study drug storage excursions to align with updates to the Pharmacy Manual, and provided updated background information related to existing treatments for Lennox-Gastaut syndrome (LGS) and additional clinical and nonclinical study data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported