STATISTICAL ANALYSIS PLAN

ZX008-1503

Zogenix International Limited
A subsidiary of Zogenix, Inc.
5959 Horton Street, [redacted]
Emeryville, CA 94608 USA

An Open-Label Extension Trial to Assess the Long-Term Safety of ZX008 (Fenfluramine Hydrochloride) Oral Solution as an Adjunctive Therapy in Children and Young Adults with Dravet Syndrome

Protocol No: ZX008-1503
Dated: 2 February 2018

Prepared by:
[redacted]
Syneos Health Clinical

STATISTICAL ANALYSIS PLAN

SIGNATURE PAGE

Zogenix International Limited
A subsidiary of Zogenix, Inc.
5959 Horton Street, [redacted]
Emeryville, CA 94608 USA

An Open-Label Extension Trial to Assess the Long-Term Safety of ZX008 (Fenfluramine Hydrochloride) Oral Solution as an Adjunctive Therapy in Children and Young Adults with Dravet Syndrome

Protocol No: ZX008-1503

Approvals

Syneos Health Approval

Name, Title	Signature	Date (DD-Mmm-YYYY)
[redacted]	[redacted] Electronically signed by: [redacted] Reason: I am the author Date: Aug 12, 2020 14:04 EDT	
[redacted]	[redacted] Electronically signed by: [redacted] Reason: I am the approver Date: Aug 12, 2020 11:13 EDT	

Zogenix International Limited Approval

Name, Title	Signature	Date (DD-Mmm-YYYY)
[redacted]	DocuSigned by: [redacted] Signer Name: [redacted] Signing Reason: I approve this document Signing Time: 06-Aug-2020 | 8:42:58 AM PDT [redacted]F03F74DFABD513FC415C2ECE2	06-Aug-2020 | 8:43:01 AM PDT
[redacted] on Behalf of Zogenix International Limited	DocuSigned by: [redacted] Signer Name: [redacted] Signing Reason: I approve this document Signing Time: 05-Aug-2020 | 9:10:07 PM PDT [redacted]28231974A8C963EED6C5D6404BE	05-Aug-2020 | 9:10:56 PM PDT

REVISION HISTORY

Date	Revision	Initials
January 16, 2017	V0.1 based on 13 September 2016 version (Protocol Amendment 1.2.1 (ROW)	RS/GAS
February 21, 2018	V1.0 Based on Amendment 3	GAS
April 6, 2018	V1.1; signatures; prior to database lock for interim	GAS
July 15, 2018	V1.2; updated to include data cutoff dates, TOC for interim; other edits	GAS
February 11, 2019	V2.0 Based on Amendment 4	GAS
April 1, 2019	V2.1 Updated TOC for TFLs to correct items missed in previous version; updated Tables 7a-7d	GAS
July 14, 2020	V2.2: Updated to include TOC for Japan sites	MLW
July 30, 2020	Version 3.0 Signed for Japan Interim Analysis	MLW
August 4, 2020	Signoff	MLW

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

ABBREVATION	DEFINITION
AE	Adverse Event
AED	Antiepileptic Drug
AESI	Adverse Event of Special Interest
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical
BID	bis in die; two times per day
BMI	Body Mass Index
BRIEF	Behavior Rating Inventory for Executive Function
C-SSRS	Columbia-Suicide Severity Rating Scale
CBD	Cannabidiol
CDISC	Clinical Data Interchange Standards Consortium
CGI	Clinical Global Impression
DS	Dravet syndrome
ECG	Electrocardiogram
ECHO	Echocardiogram
eCRF	electronic Case Report Form
EOS	End of study
EPAR	European Public Assessment Report
EQ-5D-5L	Standardized measure of health status
ET	Early Termination
FAS	Full Analysis Set
HADS	Hospital Anxiety and Depression Scale
HR	Heart Rate
IDSMC	Independent Data and Safety Monitoring Committee
IMP	Investigational Medicinal Product
IPCAB	International Pediatric Cardiology Advisory Board
IR	Incidence rate
IVR	Interactive Voice Randomization
IWR	Interactive Web Response (System)
Kg	Kilogram
Kg/ m^2	Kilogram per meter square
MCSF	Mean Convulsive Seizure Frequency
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mg/kg/day	milligram per kilogram per day
min	Minutes
mITT	modified Intent-to-Treat

ABBREVATION	DEFINITION
mL	Milliliter
MMRM	Mixed Effects Model for Repeated Measures
msec	Millisecond
OLE	Open Label Extension
OLED1	Open label Extension Day 1
PA	Protocol Amendment
PedsQL	Pediatric Quality of Life Inventory
PD	Pharmacodynamics
PK	Pharmacokinetics
PP	Per Protocol
QoL	Quality of Life
QOLCE	Quality of Life in Childhood Epilepsy
QTcF	corrected QT interval using Fredericia method
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SMEI	Severe Myoclonic Epilepsy Of Infancy
SOC	System Organ Class
T+M	Titration plus Maintenance Periods
TEAE	Treatment Emergent Adverse Event
THC	Tetrahydrocannabinol
TSH	Thyroid Stimulating Hormone
WHO-DD	World Health Organization Drug Dictionary
ZX008	Fenfluramine Hydrochloride Oral Solution

1. INTRODUCTION

ZX008 (fenfluramine hydrochloride) is under clinical development for the adjunctive treatment of patients with Dravet syndrome (DS). DS, also known as severe myoclonic epilepsy of infancy (SMEI), is a rare and severe form of epilepsy first described by Charlotte Dravet in 1978 (Dravet 1978). The condition most commonly appears during the first year of life as frequent febrile seizures. As the condition progresses, other types of seizures typically occur, including myoclonic seizures and status epilepticus (Dravet 1978). Following the appearance of these seizures, affected children develop several co-morbid conditions including psychomotor regression, ataxia, sleep disturbance, and cognitive impairment. Intellectual impairment begins to become apparent around age 2 years due to lack of intellectual/behavioral progression. Dravet children often have a lack of coordination, poor development of language, hyperactivity, and difficulty relating to others (Dravet 1978; Hurst 1990). DS is a highly treatment-resistant and refractory epilepsy syndrome. To date, only one treatment, Diacomit® (stiripentol) is approved, and only in Europe, as adjunctive therapy in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet syndrome), and must be co-administered with clobazam and valproate.

Zogenix is developing a new formulation of fenfluramine hydrochloride, ZX008, for the adjunctive treatment of DS. Studies ZX008-1501 and 1502 are two randomized controlled trials of two fixed doses of ZX008 (Fenfluramine HCl) as an adjunctive therapy in children and young adults with DS. Study 1501 is conducted in North America (Canada and the USA), and 1502 is being conducted in Europe and Australia (Australia, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, and the United Kingdom). The objective of each study is to demonstrate that ZX008 0.8 mg/kg/day is superior to placebo as adjunctive therapy in the treatment of DS in children and young adults based on change in the frequency of convulsive seizures between baseline and the combined Titration and Maintenance Periods (T+M). Study ZX008-1504 is a multicenter, 2-Cohort trial to first assess the pharmacokinetic and safety profile of a single dose of ZX008 (Fenfluramine Hydrochloride) oral solution when added to standard of care (Cohort 1), followed by a randomized, double-blind, placebo-controlled parallel group evaluation of the efficacy, safety, and tolerability of ZX008 as adjunctive antiepileptic therapy to stiripentol treatment in children and young adults with DS (Cohort 2).

The purpose of this Statistical Analysis Plan (SAP) is to outline the planned analyses and presentation of the clinical data from protocol ZX008-1503, dated 08 February2018 (amendment 4.0), an international, multicenter, open-label, long-term safety study of ZX008 in pediatric and young adult subjects with DS who have successfully completed 14 weeks of treatment in core study ZX008-1501, ZX008-1502, and ZX008-1504 Cohort 2, or successfully completed core study ZX008-1504 Cohort 1, and are candidates for continuous treatment for an extended period of time. In addition, subjects who are >18 to ≤35 years of age at the time of screening, and who meet all other eligibility criteria may be eligible for participation after discussion with the Medical Monitor and sponsor about the potential risks and benefits for receiving ZX008. Participation for these subjects will be at the discretion of the sponsor.

Amendment 3 of this clinical trial extended the initial 12-month study period to 24 months, and Amendment 4 extended the duration to 36 months. Thus, with the implementation of Amendment 4, this clinical trial will consist of an up to 36-month Open-Label Extension (OLE) Treatment Period and a 2-week Post-Dosing

Period. Subjects who complete this trial will have been treated with ZX008 for a minimum of up to 3 years (including their participation in both the core study and this study). Subjects who did not participate in one of the core studies will undergo a screening period up to 28 days to confirm eligibility prior to receiving their first dose in the OLE Treatment Period. A follow-up electrocardiogram (ECG) and echocardiogram (ECHO) will be performed at 3 and 6 months after study drug discontinuation for early termination and for those subjects who complete the study.

An earlier version of this Statistical Analysis Plan detailed statistical analyses performed as an interim analysis to support the filing of a New Drug Application (NDA) with the US Food and Drug Administration (FDA) and a Marketing Authorisation Application (MAA) with the European Medicines Agency (EMA), based on Amendment 3 of the Study Protocol. The purpose of this updated Statistical Analysis Plan is to provide details of the statistical presentation of the data from this study based on Amendment 4 of the protocol, for the 120-day safety update report following filing of the New Drug Application with the US Food and Drug Administration.

It is planned to perform an analysis of key safety data obtained up to February 15, 2019, for all subjects who entered Study ZX008-1503 by December 31, 2018.The planned interim analysis will present data without revealing the individual treatment groups from the Core studies. The specific list of TFLs that will be presented in the interim analysis will be delineated in the Table of Contents for the TFL shells.

An analysis of Study ZX008-1503 to include only those subjects who entered Study ZX008-1503 from sites in Japan (i.e., Japanese subjects) is planned when all Japanese subjects have reached at least the Month 3 visit.. Selected analyses, described in the SAP for the rest of the world, will be performed for this population.

A final analysis and report of all data obtained from this study will be provided within 6 months of completion of the last subject's final study visit.

The planned analyses identified in this SAP will be included in regulatory submissions and/or future manuscripts. Exploratory analyses not identified or defined in the SAP may be performed to support the clinical development program. Any post-hoc or unplanned analyses performed and not identified in this SAP will be documented in the CSR or final report.

2. STUDY OBJECTIVES

2.1 PRIMARY OBJECTIVE

The primary objective of the study is to assess the long-term safety and tolerability of ZX008.

2.2 SECONDARY OBJECTIVES

The secondary objectives of the study are:

- To assess the effect of ZX008 relative to the pre-ZX008 baseline on the following effectiveness measures:
  - The change in the frequency of convulsive seizures.

- The proportion of subjects who achieve a ≥ 25%, ≥ 50%, and ≥ 75% reduction in convulsive seizure frequency.
- The duration of the longest interval between convulsive seizures.
- The percentage of convulsive seizure-free days.
- The change in the frequency of non-convulsive seizures.
- The change in the frequency of convulsive + non-convulsive seizures.

- To estimate the incidence of the following on subjects receiving ZX008:
  - Use of rescue medication
  - Hospitalization to treat seizures
  - Status epilepticus
- To assess the effect of ZX0008 relative to the pre-ZX0008 baseline on the following measures:
  - Quality of Life in Childhood Epilepsy (QOLCE) score
  - The Pediatric Quality of Life Inventory (PedsQL) (Version 4.0) – Parent Report
  - PedsQL Family Impact Module (Version 2.0) – Parent Report – mITT Population
  - QoL of the parent/care giver using the EQ-5D-5L scale
  - Affective symptoms of the parent/caregiver using the HADS.
- To assess the effect of ZX0008 on the following global ratings
  - Clinical Global Impression – Improvement rating, as assessed by the principal investigator
  - Clinical Global Impression – Improvement rating, as assessed by the parent/caregiver

2.3 EXPLORATORY OBJECTIVES

Exploratory objectives of the study are the following measures that were assessed only in subjects who had participated in Study ZX008-1504, Cohort 2 as their feeder study. Additional exploratory analyses may be undertaken if warranted, as mentioned above.

- To assess the effect of ZX008 on the following measures:
  - Sleep quality and mealtime behavior, as assessed by the parent/caregiver
  - Karolinska Sleep Scale
  - Health and social care resource use (These measures include planned and unplanned hospital visits, use of ambulances, GP visits, speech and language therapy utilization, occupational and physical therapy utilization)

3. STUDY DESIGN

3.1 OVERALL STUDY DESIGN AND PLAN

This is an international, multicenter, open-label, long-term safety study of ZX008 in pediatric and young adult subjects with Dravet syndrome who have successfully completed 14 weeks of treatment in core study ZX008-1501, ZX008-1502, and ZX008-1504 Cohort 2, or successfully completed core study ZX008-1504 Cohort 1, and are candidates for continuous treatment for an extended period of time. This trial will consist of a 24-month OLE Treatment Period and a 2-week Post-Dosing Period. Thus, subjects who complete this trial will have been treated with ZX0008 for at least 1 year (including their participation in both the core study and this study).

3.2 TREATMENTS

Subjects in the double-blind studies Z008-1501, -1502, and cohort 2 of 1504 who enter Study ZX008-1503 would have transitioned to 0.2 mg/kg during the transition period (between Visits 12 and 13), as described in the 1501 and 1502 Clinical Study Protocols Section 5.5.5, and 1504 Sections 5.5.6 and 5.5.7. Subjects entering from Cohort 1 in Study ZX008-1504 will enter a transition period at a fixed dose of ZX008 0.2 mg/kg/day for up to 24 additional weeks.

In Study ZX008-1503, during the OLE Treatment Period, all subjects will be treated initially with 0.2 mg/kg/day for 1 month to assess effectiveness of this dose in all study subjects. After 1 month at a dose of 0.2 mg/kg/day, the investigator may adjust the dose of each subject based on effectiveness and tolerability. Subjects whose conditioned worsened relative to their status at the end of the double-blind feeder study could request permission to increase to 0.4 mg/kg/day (max 30mg) after approximately 2 weeks on the 0.2 mg/kg dose, Dose changes should be made in increments of 0.2 mg/kg/day, to a maximum of 0.8 mg/kg/day but not to exceed total dose of 30 mg/day. Dose increases should not occur earlier than every 14 days at each dose level. For subjects in Study ZX008-1504 Cohort 2, the dose titration schedule is 0.2 mg/kg/day, to 0.4, to 0.5 not to exceed 20 mg/day. Dose increases may only occur after a review of the diary and reported AEs, and if, in the investigator's opinion, seizure frequency, severity, and/or duration indicates a change in medication regimen is warranted. Dose decreases for tolerability can occur at the investigator's discretion, in dose amounts and frequency appropriate for the situation. ZX008 dose adjustments outside of these parameters should be discussed with the Medical Monitor prior to initiation.

Effectiveness and safety data will be provided for all subjects treated with ZX008. Data will be summarized by subjects' treatment group in their previous study.

The treatment groups that may be used to summarize the results of the final analysis are presented in Table 1. Groups 1 to 5 are the basic treatment groups.

Table 1. Treatment Groups in Study ZX008-1503 According to Treatment in Feeder Study

Name of Treatment Group	Treatment Group Code	AED Treatment from Feeder study	Feeder Study(s)	Approximate Total Number of subjects at Final Analysis
PBO-ZX008 OL	1	Placebo in feeder study along with any protocol-approved background AED combination; no active ZX008	1501, 1502, 1504 Cohort 2	120
ZX 0.2 – ZX008 OL	2	Any protocol-approved background AED combination; plus, ZX008 0.2 mg/kg/day max 30 mg	1501, 1502	80
ZX 0.8 – ZX008 OL	3	Any protocol-approved background AED combination; plus, ZX008 0.8 mg/kg/day max 30 mg	1501, 1502	80
ZX 0.5 – ZX008 OL	4	Protocol-approved background regimen including STP + VPA and/or CBZ; plus ZX008 0.5 mg/kg/day max 20 mg	1504 Cohort 2	40
PK - ZX008 OL	5	Protocol-approved background regimen including STP + VPA and/or CBZ; plus ZX008 0.5 mg/kg/day max 20 mg	1504 Cohort 1	18
ZX DBA – ZX008 OL	6 (Groups 2-4)	Any protocol-approved background regimen, plus ZX008 at any protocol-approved dose – DB Studies only		200
ZX DB – ZX008 OL	7 (Groups 1-4)	Any protocol-approved background regimen at any protocol-approved dose – DB Studies only		320
ZX – ZX008 OL	8 (Groups 2-5)	Any protocol-approved background regimen, plus ZX008 at any protocol-approved dose – All studies		218
ZX008 OL	9 (Groups 1-5)	Any protocol-approved background regimen at any protocol-approved dose – All studies		338
De Novo Subjects	10	N/A	N/A	TBD

3.3 TREATMENT PERIODS

The duration of participation in the study for an individual subject is expected to be up to 158 weeks, plus a follow-up safety visit 3 and 6 months after the last dose.

- OLE Treatment Period – 36 months (156 weeks)
- Post-Dosing Visit – 2 weeks after study completion or early termination.
- Cardiac Follow-up (ECG and ECHO) – 3 and 6 months after study drug discontinuation for early termination and for those subjects who complete the study.

3.3.1 OLE Treatment Period

Study medication will be administered as equal doses BID in the morning and in the evening approximately 12 hours apart, with food. Each dose should be separated by a minimum of 8 hours and a maximum of 12 hours. A missed dose of study medication may be taken later up to 8 hours before the next scheduled dose; otherwise, the missed dose should not be given.

Administration of the initial IMP will be based on the 0.2 mg/kg/day (maximum 30 mg/day or 20 mg/day for subjects taking concomitant STP) dose and subject's weight at Visit 1 (Study Day 1). At Visits 5 to 15 (Months 3 to 33), if the subject's weight has changed ± 25% of the weight from the previous dose calculation, the IMP dose will be recalculated. Subjects will be dosed using the oral dosing syringe provided.

During the OLE Treatment Period, all subjects will be treated initially with 0.2 mg/kg/day for 1 month to assess effectiveness of this dose in all study subjects. After 1 month at a dose of ZX008 0.2 mg/kg/day, the investigator may adjust the dose of each subject based on effectiveness and tolerability.

Dose changes should be made in increments of 0.2 mg/kg/day, as follows:

- Subjects who are not receiving concomitant STP: may increase to a maximum of 0.8 mg/kg/day but not to exceed total dose of 30 mg/day
- Subjects who are receiving concomitant STP: the first dose change will be to 0.4 mg/kg/day and the final dose change will be to 0.5 mg/kg/day, but not to exceed 20 mg/day

Additional details on dosing are provided in the clinical study Protocol.

3.3.2 Taper Period

All subjects (those who complete the OLE Treatment Period and those who discontinue from the study early) will be tapered off study medication.

3.3.2.1 Taper Period for Subjects from Core Studies ZX008-1501, ZX008-1502, and ZX008-1504 Cohort 1/Regimens 1&2

The tapering scheme is a 2-step process for subjects who are not receiving concomitant STP, including subjects from core studies ZX008-1501 and ZX008-1502, and from study ZX008-1504 Cohort 1/Regimens 1&2. This is described in Table 2.

Study medication will be administered as equal doses BID in the morning and in the evening, approximately 12 hours apart, with food. Each dose should be separated by a minimum of 8 hours and a maximum of 12 hours. A missed dose of study medication may be taken later up to 8 hours before the next scheduled dose; otherwise, the missed dose should not be given. IMP will be administered using the oral dosing syringe provided.

Table 2. Taper Algorithm for Subjects from Core Studies ZX008-1501, ZX008-1502, and ZX008-1504 Cohort 1/Regimens 1&2 Not Receiving Concomitant STP

Current Dose	Taper Step 1 Days 1-4 after study completion or early termination	Taper Step 2 Days 5-8 after study completion or early termination
ZX008 0.2 mg/kg/day	Not applicable	Not applicable
ZX008 0.4 mg/kg/day	ZX008 0.2 mg/kg/day	Not applicable
ZX008 0.6 mg/kg/day	ZX008 0.4 mg/kg/day	ZX008 0.2 mg/kg/day
ZX008 0.8 mg/kg/day	ZX008 0.4 mg/kg/day	ZX008 0.2 mg/kg/day
Note: maximum daily dose of ZX008 is 30 mg.		

Regimen 1 = **CLB + VPA + ZX008 0.2 mg/kg; Regimen 2 = CLB + VPA + ZX008 0.4 mg/kg**

3.3.2.2 Taper Period for Subjects from Core Study ZX008-1504 Cohort 1 Regimen 3 and Cohort 2

The tapering scheme is a 3-step process for subjects receiving concomitant STP, including subjects from core study ZX008-1504 Cohort 1 Regimen 3 and Cohort 2, and is described in Table 3.

Study medication will be administered as equal doses BID in the morning and in the evening, approximately 12 hours apart, with food. Each dose should be separated by a minimum of 8 hours and a maximum of 12 hours. A missed dose of study medication may be taken later up to 8 hours before the next scheduled dose; otherwise, the missed dose should not be given. IMP will be administered using the oral dosing syringe provided.

Table 3. Taper Algorithm for Subjects Receiving Concomitant STP

Current Dose	Taper Step 1 Days 1-4 after study completion or early termination	Taper Step 2 Days 5-8 after study completion or early termination	Taper Step 3 Days 9-14 after study completion or early termination
ZX008 0.2 mg/kg/day	Not applicable	Not applicable	Not applicable
ZX008 0.4 mg/kg/day	ZX008 0.2 mg/kg/day	Not applicable	Not applicable
ZX008 0.5 mg/kg/day	ZX008 0.4 mg/kg/day	ZX008 0.2 mg/kg/day	Not applicable
Note: maximum daily dose of ZX008 is 20 mg.			

Regimen 3 = **CLB + VPA + STP + ZX008 0.2 mg/kg**

Seizure data from the Taper period will not be included in the planned effectiveness endpoints except where specified. However, all safety data obtained including data obtained through the taper period, will be included in the safety analyses.

3.4 RANDOMIZATION AND BLINDING

This is an open-label study and the doses to be administered are ZX008 0.2 mg/kg to 0.8 mg/kg up to a maximum of 30 mg/day. Subjects taking concomitant STP, including subjects from Study ZX008-1504, should not exceed 0.5 mg/kg/day; with a daily maximum of 20 mg. Assignment of subject to treatment is not randomized. All subjects begin the OLE treatment period with 0.2 mg/kg for one month, after which the dose may be adjusted in increments of 0.2 mg/kg to achieve appropriate level of effectiveness/tolerability.

4. SCHEDULE OF ASSESSMENTS

Table 4. Schedule of Assessments for Subjects from Core Studies ZX008-1501 and ZX008-1502, and de Novo Subjects**

Study Assessments	OLE Treatment Period					Post-Dosing	Cardiac Follow-up
Visit Number	Visit 1[a]	Visit 2[c]		Visits 3-15 (Months 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33)	Visit 16[d] (EOS/ET) Month 36	Visit 17	Visit 18, 19
Study Day	-28 to 1[a]	15		30, 60, 90, 180, 270, 365, 455, 545, 635, 725. 815, 905, 995	1085	1099	3 and 6 months post last dose
		Clinic	Phone				
Informed Consent	X						
Entry Criteria	X						
Demographics	X						
Medical/Neurological History	X[a]						
Epilepsy History	X[a,b]						
Physical Examination, complete	X[a]				X		X[e]
Physical Examination, abbreviated		X		X			X[e]
Neurological Examination, complete	X[f]				X		
Neurological Examination, abbreviated		X		X			
Vital signs	X	X		X	X		
Weight, Height, BMI	X[a]	X		X	X		
12-lead ECG	X[a]			X	X		X[e]
Doppler ECHO	X[a]			X[g,h]	X		X[e]
Urine Pregnancy Test[h]	X			X	X		
Clinical laboratory evaluation (hematology/clinical chemistry/urinalysis, etc)	X[j]	X[j]		X	X		
Urine THC Panel/Whole blood CBD	X[a]			X	X		
Plasma sample for background AEDs		X		X	X		
Tanner Staging (for subjects >7 to ≤ 18 years)	X[a]			X[k]	X		X[k]
C-SSRS	X[a]			X	X		
CGI-I (assessed by parent/caregiver)	X[a]			X	X		
CGI-I (assessed by principal investigator)	X[a]			X	X		
QOLCE	X[a]			X	X		
EQ-5D-5L (QoL of parent/caregiver)	X[a]			X	X		
HADS (Affect of parent/caregiver)	X[a]			X	X		
BRIEF	X[a]			X	X		

continued

Table 4. Schedule of Assessments for Subjects from Core Studies ZX008-1501 and ZX008-1502, and de Novo Subjects (continued)**

Study Assessments	OLE Treatment Period					Post-Dosing	Cardiac Follow-up
Visit Number	**Visit 1[a]**	**Visit 2[c]**		**Visits 3-15 (Months 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33)**	**Visit 16[c] (EOS/ET) Month 36**	**Visit 17**	**Visit 18, 19**
Study Day	**-28 to 1[a]**	**15**		**30, 60, 90, 180, 270, 365, 455, 545, 635, 725. 815, 905, 995**	**1085**	**1099**	**3 and 6 months post last dose**
		Clinic	**Phone**				
PedsQL [n]	X[a]			X	X		
Study medication palatability assessment				X[l]			
Subject Diary	D	C/R/D	R	C/R/D	C/R	C/R	
Study Medication	D[b]	C/R/D	R	C/R/D	C/R/D	C/R	
Daily Diary Completion	----------	----------	----------	X	----------	----------	
Concomitant Medication	X[a]	----------	----------	X	----------	----------	
Adverse Events	X[a]	----------	----------	X	----------	----------	
Adverse events of special interest	X[a]	----------	----------	X	----------	----------	X[m]

AED=antiepileptic drug; BMI=body mass index; BRIEF=Behavior Rating Inventory of Executive Function; C=Collect; CBD=cannabidiol; CGI-I=Clinical Global Impression-Improvement; D=Dispense; ECG=electrocardiogram; EOS=end of study; ET=early termination; EQ-5D-5L=standardized measure of health status; HADS=Hospital Anxiety and Depression Scale; PedsQL=Pediatric Quality of Life Inventory; QoL=quality of life; QOLCE=Quality of Life in Childhood Epilepsy; R=Review

NOTE: If a subject has a birthday during the study that makes a previously unrequired assessment now required (eg, Tanner staging in a male subject who turns 8 years old during the study), this assessment(s) should be initiated at visits subsequent to the birthday.

**** de Novo subjects are subjects who did not participate in one of the core studies and may or may not be currently taking STP.**

a: For subjects enrolling from one of the core studies use data collected at Visit 12 and Visit 13 of Study ZX008-1501 or ZX008-1502.
For de novo subjects, a screening period up to 28 days is required. During this period, informed consent is required prior to any study-related procedures. All results to determine eligibility must be reviewed prior to receiving the first dose of study medication at Visit 1.
For all subjects, clinical laboratory results and all ECHO/ECG results must be available and meet eligibility criteria prior to receiving the first dose of study medication at Visit 1.

b: De Novo subjects must meet entry criteria 3 to 7, and 10, including having had ≥4 convulsive seizures (tonic, tonic-atonic, tonic-clonic, clonic) per 4-week period for past 12 weeks prior to screening, by parent/guardian report to investigator or investigator medical notes.

c: At the discretion of the investigator, Visit 2 may be conducted as a phone visit.

d: Or early termination.

e; Follow-up ECG, ECHO, and physical examination will be performed 3 and 6 months after study completion or early termination.

f: For subjects enrolling from one of the core studies, use core study Visit 12 information unless complete neurological examination is warranted based on significant changes in subject status.

g: ECHOs will be performed at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33.

h: The Months 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33 ECHO may be performed any time within 3 weeks prior to the study visit. If a subject discontinues early from the study, the ECHO should be scheduled as soon as practical (see Table 7).

i: Females of child-bearing potential

j: For subjects enrolling from one of the core studies, use data collected at Visit 12 of ZX008-1501 or ZX008-1502 for Visit 1 unless clinical laboratory evaluation is warranted based on significant changes in subject status. Visit 2 clinical laboratory evaluation is optional based on subject status for all cohorts.

k: Months 6, 15, and 27 only.

l: Visits 3 and 4 (Months 1 and 2) only.

m: Only adverse events related to cardiac safety will be collected at this visit (see Table 7).

n: Not to be completed for de novo subjects >18 years old.

Table 5. Schedule of Assessments for Subjects from Core Study ZX008-1504

Study Assessments	OLE Treatment Period					Post-Dosing	Cardiac Follow-up
Visit Number	Visit 1[a]	Visit 2[b]		Visits 3-15 (Months 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33)	Visit 16[c] (EOS/ET) Month 36	Visit 17	Visit 18, 19
Study Day	1[a]	15		30, 60, 90, 180, 270, 365, 455, 545, 635, 725. 815, 905, 995	1085	1099	3 and 6 months post last dose
		Clinic	Phone				
Informed Consent	X						
Entry Criteria	X						
Demographics	X						
Medical/Neurological History	X[a]						
Epilepsy History	X[a]						
Physical Examination, complete	X[a]				X		X[d]
Physical Examination, abbreviated		X		X			X[d]
Neurological Examination, complete	X[e]				X		
Neurological Examination, abbreviated		X		X			
Vital signs	X	X		X	X		
Weight, Height, BMI	X[a]	X		X	X		
12-lead ECG	X[a]			X	X		X[d]
Doppler ECHO	X[a]			X[f,g]	X		X[d]
Urine Pregnancy Test[h]	X			X	X		
Clinical laboratory evaluation (hematology/clinical chemistry/urinalysis, etc)	X[i]	X[i]		X	X		
Urine THC Panel/Whole blood CBD	X[a]			X	X		
Plasma sample for background AEDs		X		X	X		
Tanner Staging (for subjects > 7 years old)	X[a]			X[j]	X		X[j]
C-SSRS	X[a]			X	X		
CGI-I (assessed by parent/caregiver)	X[a]			X	X		
CGI-I (assessed by principal investigator)	X[a]			X	X		
QOLCE	X[a]			X	X		
EQ-5D-5L (QoL of parent/caregiver)	X[a]			X	X		
BRIEF	X[a]			X	X		
Healthcare utilization questions	X[a]			X	X		

continued

Table 5. Schedule of Assessments for Subjects from Core Study ZX008-1504 (continued)

Study Assessments	**OLE Treatment Period**					**Post-Dosing**	**Cardiac Follow-up**
Visit Number	**Visit 1[a]**	**Visit 2[b]**		**Visits 3-15 (Months 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33)**	**Visit 16[c] (EOS/ET) Month 36**	**Visit 17**	**Visit 18, 19**
Study Day	**1[a]**	**15**		**30, 60, 90, 180, 270, 365, 455, 545, 635, 725. 815, 905, 995**	**1085**	**1099**	**3 and 6 months post last dose**
		Clinic	**Phone**				
Karolinska Sleep Scale	X[a]			X	X		
Sleep quality/mealtime behavior questions	X[a]			X	X		
PedsQL	X[a]			X	X		
Study medication palatability assessment				X[k]			
Subject Diary	D	C/R/D	R	C/R/D	C/R	C/R	
Study Medication	D[b]	C/R/D	R	C/R/D	C/R/D	C/R	
Daily Diary Completion	----------			X		----------	
Concomitant Medications	X[a]	----------		X		----------	
Adverse Events	X[a]	----------		X		----------	
Adverse events of special interest	X[a]	----------		X		----------	X[l]

AED=antiepileptic drug; BMI=body mass index; BRIEF=Behavior Rating Inventory of Executive Function; C=Collect; CBD=cannabidiol; CGI-I=Clinical Global Impression-Improvement; D=Dispense; ECG=electrocardiogram; EOS=end of study; ET=early termination; EQ-5D-5L=standardized measure of health status; HADS=Hospital Anxiety and Depression Scale; PedsQL=Pediatric Quality of Life Inventory; QoL=quality of life; QOLCE=Quality of Life in Childhood Epilepsy; R=Review

NOTE: If a subject has a birthday during the study that makes a previously unrequired assessment now required (e.g., Tanner staging in a male subject who turns 8 years old during the study), this assessment(s) should be initiated at visits subsequent to the birthday.

a: For subjects from the core Study ZX008-1504 Cohort 1, use data collected at the last visit of the transition period; for subjects from core Study ZX008-1504 Cohort 2 use data collected at the Visit 12 and Visit 13.
For de novo subjects, a screening period up to 28 days is required. During this period, informed consent is required prior to any study-related procedures. All results to determine eligibility must be reviewed prior to receiving the first dose of study drug at Visit 1.
For subjects from ZX008-1504 Cohort 2 and de novo subjects, clinical laboratory, ECHO, and ECG results must be available and meet eligibility criteria prior to receiving the first dose of study drug at Visit 1.

b: At the discretion of the investigator, Visit 2 may be conducted as a phone visit.

c: Or early termination.

d: Follow-up ECG, ECHO, and physical examination will be performed 3 and 6 months after study completion or early termination.

e; Unless complete neurological examination is warranted based on significant changes in subject status, use data collected at the last visit of the transition period of Study ZX008-1504 Cohort 1 and for subjects from Study ZX008-1504 Cohort 2, use data collected at the Visit 12.

f: ECHOs will be performed at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33.

g: The Months 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, and 33 ECHO may be performed any time within 3 weeks prior to the study visit. If a subject discontinues early from the study, the ECHO should be scheduled as soon as practical (see Table 7).

h: Females of child-bearing potential

i: Unless clinical laboratory evaluation is warranted based on significant changes in subject status, use data collected at the last visit of the transition period of Study ZX008-1504 Cohort 1; for subjects from Study ZX008-1504 Cohort 2, use data collected at the Visit 12. For Visit 2, clinical laboratory evaluation is optional based on subject status.

j: Months 6, 15, and 27.

k: Visits 3 and 4 (Months 1 and 2) only.

l: Only adverse events related to cardiac safety will be collected at this visit (see Table 7).

5. ANALYSIS POPULATIONS

5.1 ENROLLED POPULATION

The enrolled population includes all subjects who gave informed consent or assent for entry into Study ZX008-1503.

5.2 SAFETY (SAF) POPULATION

The SAF population is the set of all enrolled subjects who received at least one dose of ZX008 during the open label extension. Safety analyses will be performed on the SAF Population.

5.3 MODIFIED INTENT-TO-TREAT (MITT) POPULATION

The mITT Population is defined as all enrolled subjects who receive at least one dose of ZX008 and have at least one month (30 days) of valid seizure data during the open label extension. Effectiveness analyses, such as evaluating the change in the frequency of convulsive seizures, will be performed on the mITT Population.

6. STATISTICAL METHODOLOGY

6.1 STATISTICAL AND ANALYTICAL ISSUES

6.1.1 Statistical Methods

All data on safety, effectiveness and exploratory endpoints will be summarized. Continuous data will be summarized using descriptive statistics including number of subjects, means, standard deviations, medians, lower and upper quartiles, and ranges. Categorical variables will be summarized with frequencies and percentages.

Effectiveness and safety data may be summarized by treatment group in previous study as described in Section 3.2 in this SAP. The effectiveness and safety data will also be summarized by age group as described in Section 6.1.3, and overall.

Point and interval estimates (95% confidence intervals) will be calculated for within treatment changes from baseline for key parameters as warranted. These within-treatment changes from baseline comparisons should be interpreted with caution, as any effect of treatment may be confounded with the time-course of disease or other factors. The primary evidence for efficacy and safety of ZX008 is based on the treatment comparisons from the double-blind studies, while the data from this OLE study provides evidence of long-term safety and effectiveness.

Confidence intervals and/or p-values, where provided for between treatment group differences, should be regarded as descriptive and not for formal inferential purposes.

All descriptive statistical analyses will be performed using SAS statistical software (Version 9.3, unless otherwise noted). Adverse events will be coded using the most recent MedDRA version available at the time of analysis. Concomitant medications will be coded using the most recent version of World Health Organization (WHO) Drug.

6.1.2 Multiplicity Issues

This is an open-label extension study with no formal comparisons to be made between treatment groups defined by subjects' initial regimen in the previous study. Comparisons will be made within each treatment group comparing measurements observed during different time points in the OLE to the measurements obtained during the baseline period in the double-blind or PK study completed prior to this OLE.

Confidence intervals presented for descriptive purposes only will each have nominal 95% coverage probability.

No formal adjustment for multiplicity is made.

6.1.3 Subgroups

Effectiveness and select safety data may be further broken down by the following subgroups:

- Age strata (based on age at informed consent at core study entry or entry de novo): 2 to <6 years, ≥6 – 18 years.
- Region: Countries may be grouped into two regions: North America (US/Canada), Rest-of-World (ROW).
- Japan: Subjects enrolled from Japan are considered as a separate subgroup.

6.1.4 Definitions

6.1.4.1 Baseline (Core)

For de novo subjects, the baseline (core) is undefined. For other subjects, the baseline (core) is defined as follows.

For effectiveness endpoints (excluding seizure), the baseline (core) will be defined dependent on their core study. For subjects from ZX008-1501, ZX008-1502, or ZX008-1504 Cohort 2, baseline (core) is the last value prior to randomization in the preceding double-blind study. For subjects from ZX008-1504 Cohort 1, baseline (core) is the last value prior to the start of PK dosing and assessments. For De Novo subjects, the baseline is the last value prior to dosing in ZX008-1503.

For all subjects in Study ZX008-1501, Study ZX008-1502, or Study ZX008-1504 Cohort 2, the baseline (core) period is equivalent to the core study pre-randomization period, i.e., the approximately 42-day span just prior to randomization and start of treatment in the core study. The baseline (core) seizure frequency will be based on the information collected from their daily diaries during the baseline period (lasting approximately 42 days).

For subjects from Study ZX008-1504 Cohort 1 the baseline (core) for efficacy rating scales (e.g. questionnaires) will be the last rating prior to start of dosing in the Core Study. Baseline seizure frequency for Study ZX008-1504 Cohort 1 will not be calculated.

6.1.4.2 Baseline (OLE)

Baseline (OLE) value for the Open-label treatment period is defined as the last assessment on or before the start of the OLE period. In most cases, (though not seizure frequency) this will be the value obtained at Visit 1 (Study Day 1) of Study ZX008-1503.

Thus, Baseline (OLE) lab, vital signs, ECG, ECHO, assessments refer to the assessments obtained on this day, as does Baseline (OLE) value for effectiveness endpoints with the exception of seizures.

For de novo subjects, the baseline (OLE) seizure frequency will be based on the information collected from their daily diaries during the baseline period (lasting approximately 28 days) prior to first dose in ZX008-1503.

6.1.4.3 Open-Label Extension (OLE) Treatment Period

The OLE Treatment Period covers the 36 months during which subjects will receive open label treatment with ZX008.

For each subject, OLE day 1 (OLED1) is the subject's first day of dosing in the OLE period. Study day for 1503 begins with OLED1.

6.1.4.4 Post-dosing Period

The Post-dosing Period begins immediately at the end of OLE Treatment Period and extends for 2 weeks.

6.1.4.5 Follow-up Period

Subjects are to return for an ECHO and ECG assessment 3 and 6 months after the end of the study. The follow-up period begins the day after Visit13 and ends with Visit15.

6.1.5 Other Definitions

6.1.5.1 Phase and Study Day Definitions

The analyses will require definition of 3 Phases: Pre-OLE, OLE, and Post-OLE.

- The pre-OLE Phase comprises (1) the baseline (Core) period, (2) the Core Study (CS) period (including the transition period in the core study)
- The OLE Phase starts from dosing on OLED1 and comprises (1) the OLE Treatment Period, and (2) the Taper Period. The last day of the OLE phase is the date of Visit 17.
- The post-OLE phase begins one day after the date of Visit 17 in 1503 and ends with the date of Visit 19.

Study Day 1 is the date of first dose in the OLE Study. In most cases, this will be the date of Visit 1 or the day after that date.

6.1.6 Visit Windows and Period Start/Stop Dates

The following definitions of phase and period will be used:

Table 6. Definition of Phase/Period

Phase	Period	Description
Pre-OLE Phase	Baseline (Core) Period	This description here applies to all subjects except the de novo subjects. This period refers to the period prior to the beginning of the double-blind period in the Core study. The Baseline (Core) period start date is the date of Visit 1 in the Core study. The Baseline (Core) period end date is the date of Visit 3/randomization in the Core study. For subjects in Study ZX008-1504 (Cohort 1), the baseline period starts and ends on the date of Visit 1.
Pre-OLE Phase	Core Study Period	This description here applies to all subjects except the de novo subjects. The start date of this period is the date of randomization or first dose in the Core (double-blind) study, whichever occurs first. The end date of this period is the last date the subject was on study treatment. For subjects entering Study ZX008-1503 who completed Core studies ZX008-1501, ZX008-1502 or ZX008-1504 Cohort 2, this will be the date of Visit 13 in the core study. For subjects who discontinue early from the Core study, the Core study period end date is the latest assessment date for that study. For subjects entering ZX008-1503 who were in ZX008-1504 Cohort 1, this will be the date of the Visit 17 assessment in Study 1504 Cohort 1 (for those who completed), or the date of the latest assessment date (for those who discontinued ZX008-1504 Cohort 1 prematurely but were allowed entry into 1503, if any).
Pre-OLE Phase	Baseline (OLE) Period – de novo subjects	This description here applies to the de novo subjects. This start date of this period be the date of screening. The end date of the period will be the last date prior to the first dose of study drug in Study ZX008-1503.
OLE Phase	OLE Treatment Period	The OLE Treatment Period consists of the 36-month period from Visit 1 of the OLE study through Visit 16 of the OLE study The OLE Treatment Period start date is the date of first dose in Study ZX008-1503. The OLE Treatment Period end date is the date of end of study visit, Visit 16/ET. For subjects who discontinue early from the study, the OLE Treatment Period end date will be the date of the ET visit - safety measures collected at the last clinic visit will be used even in the event that study drug was discontinued prior to the date of the visit. Note: Adverse events occurring up to Visit 17 are regarded as occurring during treatment. In addition, AEs occurring up to 30 days after the last dose date will be regarding as treatment emergent.
OLE Phase	Taper Period	The Taper period consists of 2 weeks starting from end of study/early termination visit (Visit 16) + 1 day. The end date of this period is the date recorded for Visit 17.
Post-OLE Phase	Post-OLE Period	The start date of the post-OLE period is the date of Visit 17, + 1 day for subjects who complete the OLE Treatment period, or the day after the date of end of taper, for subjects who discontinue early. [There is not explicit end date for the post-OLE Phase. However, if needed, this may be set to be 45 days after the date of Visit 19, or V17 date + 210.]]

For the purpose of statistical analysis, visit windows around the target visit dates will be implemented to capture effectiveness and/or safety data within similar periods. These windows are distinct from the

permissible visit scheduling windows specified in the Visit Schedule in the protocol that are used for the conduct of the study.

The following rules will be used to window data into treatment periods for tabulations that are generated by time during the OLE Treatment period.

Table 7a. Time Intervals for Analysis Visits for Seizure Analysis*

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit**	Time Interval (label on output)	Time Interval (Day)
Pre-OLE	N/A	-99	Baseline (Core)*	Core Study Day -42 to Day-1 of Core Study
Pre-OLE	N/A	-9	Core Study (T+M)*	Day1 of Core Study to End of T+M in Core Study
Pre-OLE	N/A	-1	Core Study Final * Week	End of T+M in Core Study – 6 days, to End of T+M in Core Study
Pre-OLE de novo	N/A	-99	Baseline (OLE)*	Day -28 to Day -1 of Study ZX008-1503
OLE	3	1	Month 1 (OLE)	1-30
OLE	4	2	Month 2 (OLE)	31-60
OLE	5	3	Month 3 (OLE)	61-90
OLE	6		Month 4-6 (OLE)	91-180
OLE	7	5	Month 7-9 (OLE)	181-270
OLE	8	6	Month 10-12 (OLE)	271-360
OLE	9	7	Month 13-15 (OLE)	361-450
OLE	10	8	Month 16-18 (OLE)	451-540
OLE	11	9	Month 19-21 (OLE)	541-630
OLE	12	10	Month 22-24 (OLE)	631-730
OLE	13	11	Month 25-27 (OLE)	731-820
OLE	14	12	Month 28-30 (OLE)	821-910
OLE	15	13	Month 31-33 (OLE)	911-1000
OLE	16	14	Month 34-36 (OLE)	1001-1095
OLE	NA	99	Month 01-EOS (ENDPT1)	1 to min(Last Dose date, Visit 16 date)
OLE	NA	98	Month 02-EOS (ENDPT2)	31 to min(Last Dose date, Visit 16 date)

Note: EOS/ET date = Visit16 date. Per protocol, Visit 17 is end of the OLE Phase.
T+M=Titration + Maintenance in Core Study.
*Subjects in Study ZX008-1504 Cohort 1 will not have a baseline(core), For those subjects, the Core Study(T+M) represents all their seizure data during the transition period in the core study. Their core study final week will be the last 7 days of seizure data prior to the first visit in ZX008-1503. De novo subjects start Study ZX008-1503 treatment after a screening period.
**Analysis visit numbers are not the same as nominal visit numbers.

Table 7b. Time Intervals for Questionnaires*

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit Number*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
Pre-OLE	N/A	-99	Baseline (Core)	<1	Core Study Day -42 to Day-1 of Core Study
Pre-OLE	1	1	Baseline (OLE)	1	1
OLE	3	3	Month 1 (OLE)	21 to 44	30
OLE	4	4	Month 2 (OLE)	45 to 74	60
OLE	5	5	Month 3 (OLE)	75 to 134	90
OLE	6	6	Month 6 (OLE)	135 to 224	180
OLE	7	7	Month 9 (OLE)	225 to 314	270
OLE	8	8	Month 12 (OLE)	315 to 409	365
OLE	9	9	Month 15 (OLE)	410 to 499	455
OLE	10	10	Month 18 (OLE)	500 to 589	545
OLE	11	11	Month 21 (OLE)	590 to 679	635
OLE	12	12	Month 24 (OLE)	680 to 774	730
OLE	13	13	Month 27 (OLE)	775 to 864	820
OLE	14	14	Month 30 (OLE)	865 to 954	910
OLE	15	15	Month 33 (OLE)	955 to 1044	1000
OLE	16	16	Month 36 (OLE)	1045 to 1109	1095
OLE	OLE Last Visit**	99	Last Value	Day 2 to Visit 17 date	

*For multiple measurements within a time window, please use the closest to the target time point. Note that measurements occurring on the end date of a phase/period or start date of a new phase/period are assigned to the preceding phase/period. For example, measurements taken on OLE Study Day1 are assigned as Baseline (OLE).
**The last observation in the time window will be used. *[This is an exception from the rule in the preceding note.]*

Table 7c. Time Intervals for Analysis Visits for Laboratory Data and Vital Signs*

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit Number*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
Pre-OLE	1	1	Baseline (OLE)	1	1
OLE	2	2	Week 2 (OLE)	2 to 20	15
OLE	3	3	Month 1 (OLE)	21 to 44	30
OLE	4	4	Month 2 (OLE)	45 to 74	60
OLE	5	5	Month 3 (OLE)	75 to 134	90
OLE	6	6	Month 6 (OLE)	135 to 224	180
OLE	7	7	Month 9 (OLE)	225 to 314	270
OLE	8	8	Month 12 (OLE)	315 to 409	365
OLE	9	9	Month 15 (OLE)	410 to 499	455
OLE	10	10	Month 18 (OLE)	500 to 589	545
OLE	11	11	Month 21 (OLE)	590 to 679	635
OLE	12	12	Month 24 (OLE)	680 to 774	730
OLE	13	13	Month 27 (OLE)	775 to 864	820

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit Number*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
OLE	14	14	Month 30 (OLE)	865 to 954	910
OLE	15	15	Month 33 (OLE)	955 to 1044	1000
OLE	16	16	Month 36 (OLE)	1045 to 1109	1095
OLE	OLE last Visit**	99	Last Value	Day 2 to Visit 17 date	

*For multiple measurements within a time window, please use the closest to the target time point. Note that measurements occurring on the end date of a phase/period or start date of a new phase/period are assigned to the preceding phase/period. For example, measurements taken on OLE Study Day1 are assigned as Baseline (OLE).
**The last observation in the time window will be used. *[This is an exception from the rule in the preceding note.]*

Table 7d. Time Intervals for Analysis Visits for Tanner Staging*

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit Number*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
Pre-OLE	1	1	Baseline (OLE)	1	1
OLE	2	2	Week 2 (OLE)	2 to 20	15
OLE	3	3	Month 1 (OLE)	21 to 44	30
OLE	4	4	Month 2 (OLE)	45 to 74	60
OLE	5	5	Month 3 (OLE)	75 to 134	90
OLE	6	6	Month 6 (OLE)	135 to 224	180
OLE	7	7	Month 9 (OLE)	225 to 314	270
OLE	8	8	Month 12 (OLE)	315 to 409	365
OLE	9	9	Month 15 (OLE)	410 to 499	455
OLE	10	10	Month 18 (OLE)	500 to 589	545
OLE	11	11	Month 21 (OLE)	590 to 679	635
OLE	12	12	Month 24 (OLE)	680 to 774	730
OLE	13	13	Month 27 (OLE)	775 to 864	820
OLE	14	14	Month 30 (OLE)	865 to 954	910
OLE	15	15	Month 33 (OLE)	955 to 1044	1000
OLE	16	16	Month 36 (OLE)	1045 to 1109	1095
OLE	17/OLE Last Visit**	99	Last Value	Day 2 to Visit 17 date	

*For multiple measurements within a time window, please use the closest to the target time point. Note that measurements occurring on the end date of a phase/period or start date of a new phase/period are assigned to the preceding phase/period. For example, measurements taken on OLE Study Day1 are assigned as Baseline (OLE). Visits where the Tanner Stage is not scheduled for collection are included due to early termination visits occurring between scheduled visits.
**The last observation in the time window will be used. *[This is an exception from the rule in the preceding note.]*

Table 7e. Time Intervals for ECGs and ECHO*

Analysis Phase/Period	Scheduled Visit Number in ZX008-1503	Analysis Visit*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
Pre-OLE	1	1	Baseline (OLE)	<1	1
OLE	3	3	Month 1 (OLE)	2 to 44	30
OLE	4	4	Month 2 (OLE)	45 to 74	60
OLE	5	5	Month 3 (OLE)	75 to 134	90
OLE	6	6	Month 6 (OLE)	135 to 224	180
OLE	7	7	Month 9 (OLE)	225 to 314	270
OLE	8	8	Month 12 (OLE)	315 to 409	365
OLE	9	9	Month 15 (OLE)	410 to 499	455
OLE	10	10	Month 18 (OLE)	500 to 589	545
OLE	11	11	Month 21 (OLE)	590 to 679	635
OLE	12	12	Month 24 (OLE)	680 to 774	730
OLE	13	13	Month 27 (OLE)	775 to 864	820
OLE	14	14	Month 30 (OLE)	865 to 954	910
OLE	15	15	Month 33 (OLE)	955 to 1044	1000
OLE	16	16	Month 36 (OLE)	1045 to 1109	1095
OLE	17/Final Visit**	99	Last Value	2 to Visit 17 date	
Post-OLE	18	999	Cardiac FU 1	Visit 17 date + 1, to Visit 18 date	
Post-OLE	19	9999	Cardiac FU 2	Visit 18 date +1, to Visit 19 date	

*For multiple measurements within a time window, please use the closest to the target time point. Note that measurements occurring on the end date of a phase/period or start date of a new phase/period are assigned to the preceding phase/period. For example, measurements taken on OLE Study Day1 are assigned as Baseline (OLE).
** The last observation in the time window will be used. *[This is an exception from the rule in the preceding note.]*

6.1.7 Handling of Dropouts and Missing Data

6.1.7.1 Missing Data

There will be no explicit imputation of missing data for effectiveness endpoints.

6.1.7.2 Seizure Diaries

Seizures are recorded in the Daily Seizure Diary, while the End of Day Diary provides Yes/No confirmation that that seizures were experienced for a specific date, or that the date was seizure free.

- If no seizures are entered in the DSD and the EDD confirms seizure freedom, the number of seizures for that date is zero.
- If seizures are entered in the DSD and the EDD states seizures freedom, the seizures recorded for that date supersede the EDD stating seizure freedom.
- If no seizures are entered in the DSD and there is no response in the EDD, that day will be considered to have missing diary data.
- If no seizures are entered in the DSD and there is a Yes response in the EDD, that day will be considered to have missing diary data.

Handling of missing date information for AEs:

- The term *missing date* refers to a completely missing date or to an incomplete date/partial date where parts are not available, e.g. missing month/day/year.
- Missing start and end date will be imputed conservatively, i.e. missing values will be imputed in such a way that the duration of the AE is considered with the longest possible duration and such that, whenever the AE may potentially start after first IMP, the AE will be handled as a TEAE.
- The missing start date and end date of AE will be imputed for the purpose of calculating treatment emergent status and assigning events to treatment periods using definitions given in the following table.

Table 8 Data Conventions for Missing Adverse Event Start or Stop Dates

Start or End Date Missing	Data Convention
Partial /Missing Start date	Missing day – If Adverse event day is missing but month and year are present then Impute the 1st of the month unless month is same as month of first dose of study drug then impute first dose date. Missing day and month – If adverse event day and month are both missing but year is present then impute 1st January unless year is the same as first dose date then impute first dose date. Completely missing – impute first dose date unless the end date suggests it could have started prior to this in which case impute the 1st January of the same year as the end date. When imputing a start date, ensure that the new imputed date is sensible i.e. is prior to the end date of the AE.
Partial /Missing End date	If the AE is "ongoing", do not impute an end date. The following applies to a missing end date where the AE is not "ongoing": Missing day – If AE end day is missing but month and year are present then Impute the last day of the month unless month is same as month of last dose of study drug then impute last dose date. Missing day and month – If AE has missing day and month but year is present then impute 31st December unless year is the same as the last dose date then impute last dose date. Completely Missing – need to look at whether the AE is still ongoing before imputing a date and when it started in relation to study drug. If the ongoing flag is missing then assume that AE is still present (i.e. do not impute a date). If the AE has stopped and start date is prior to first dose date then impute the 1st dose date, if it started on or after first dose date then impute a date that is after the last dose date.

6.1.8 Conversion of Time Interval

In case a time interval was calculated in days and needs to be converted into weeks, months or years the following conversion factors need to be used:

1 week = 7 days

1 month = 30.4 days

1 year = 365.25 days

6.1.9 Pooling of Investigative Sites

Sites participating in this study are from Australia, Europe and North America. Due to the small numbers of subjects at each site, there is no plan to use site as a stratifying factor in the analyses; the primary analysis will use data pooled across site. The effectiveness and safety analyses may be presented by region.

6.1.10 Determination of Sample Size

The sample size justification as indicated in the study protocol is as follows: The sample size will be determined by the number of subjects in the three core studies (Study ZX008-1501, Study ZX008-1502, or Study ZX008-1504) who volunteer for the extension study and meet the necessary criteria for enrollment. Approximately 100-120 subjects are expected to participate in each of the core studies. Thus, if all of those participants also enrolled in the extension, the total sample size of the extension study would be between 300 and 360.

It is expected that this sample size will provide adequate exposure information for this orphan drug, to inform the label at time of marketing authorization, and would allow detection of at least one, two or three rare events with reasonable likelihood. As an example, if a slightly conservative estimate of the number of subjects enrolled in Study ZX008-1503 is set at n=270, the table below provides probability calculations for detecting at least one, 2, or 3 events, assuming various values for an underlying event rate of 1, 2, 3, 4, 5, or 10%:

Table 9: Probability calculations for specified adverse event occurrence rates

	Probability of detecting an adverse event in trial with n=270, with specified true event rate of:					
Probability of observing	10%	5%	4%	3%	2%	1%
≥1 event	100.0	100.0	99.998	99.97	99.6	93.4
≥2 events	100.0	99.999	99.98	99.7	97.2	75.3
≥3 events	100.0	99.989	99.88	98.8	90.7	50.7

6.2 SUBJECT CHARACTERISTICS

Individual subject data will be listed for all subjects in the SAF population. Unless otherwise specified, all data summaries will be overall and by Core study treatment group as described in Section 3.2 of this SAP.

6.2.1 Subject Disposition

Subject disposition will be presented for all subjects overall, and by treatment group in Core study for the Enrolled and SAF populations. Disposition information that will be summarized includes number of subjects who started treatment in the OLE study, number who withdrew prematurely, and reasons for withdrawal.

6.2.2 Protocol Deviations

Protocol deviations will be reviewed, and those deviations that are regarded as major will be summarized. Major protocol deviations affecting effectiveness or safety assessment may include:

- Non-compliance regarding intake of IMP
- Inappropriate intake of concomitant medication or background AEDs
- Other non-compliance

Multiple deviations can occur in the same subject and thus a subject can be counted in more than one deviation category.

All protocol deviations will be presented in a subject data listing for the SAF population sorted by subject within study site.

6.2.3 Background and Demographic Characteristics

Subject demographics and baseline characteristics will be summarized for the SAF and mITT.

6.2.3.1 Subject Demographics/Baseline Characteristics

The following demographic characteristics will be summarized for the data at entry into 1503:

- Age at Core Study entry [Years] / for de novo subjects, this will be the age at entry into 1503
- Age Category(<6 years or ≥6 years)
- Sex
- Race
- Ethnicity
- Height [m]
- Weight [kg]
- BMI [kg/m^2]

All subject demographics data will be listed for the SAF populations.

6.2.3.2 Other Baseline Characteristics

Epilepsy/seizure history will be descriptively summarized as per data type (continuous or categorical).

All subject baseline characteristics will be listed for the SAF population.

6.2.4 Treatment Exposure and Compliance

6.2.4.1 Treatment Exposure

Treatment exposure data will be summarized for subjects' time on treatment in Study ZX008-1503 only and analyzed for the SAF population.

Duration of total exposure to fenfluramine hydrochloride (i.e., time on treatment (in days)) will be calculated per subject as the number of days with IMP intake during the trial, as follows:

Duration of exposure = Date of last IMP intake – Date of first IMP intake + 1

The number of days exposed to fenfluramine hydrochloride will be summarized overall and by treatment group using n, mean, standard error, median, minimum, Q_1, Q_3 and maximum.

The actual dose of medication consumed will be calculated and summarized overall and by treatment group using n, mean, standard error, median, minimum, Q_1, Q_3 and maximum.

The shift in dosage of ZX008 will be presented at each scheduled visit starting from Visit 3 – OLE Month 1 and going to Visit 16 – OLE Month 36 or End of Study. At the visit, the number of subjects who attended the visit will be provided with the dosage of ZX008 assigned to the subject at the last study drug dispense prior to the visit and the dosage of ZX008 assigned at the conclusion of the visit.

The duration of exposure to fenfluramine hydrochloride will be summarized in monthly periods based on the mean daily dosage in mg/kg/day and in mg/day. In addition, the duration of time in days based on the assigned dosage in mg/kg/day will be summarized. For the actual dosage summary, the periods where a subject has had a particular dosage assigned may not be concurrent.

6.2.4.2 Compliance to IMP Intake

Study medication is to be administered twice daily, and compliance is recorded in the eDiary as full (both doses), partial (less than full daily dose) or missed (both doses) each day. From this, compliance to IMP intake will be calculated by assuming that a missed dose=0% of dose consumed, partial=50% of dose consumed, and full=100% of dose consumed. For each subject, a daily compliance score will be thus obtained.

Compliance will be summarized for the SAF and mITT populations.

6.2.5 Prior and Concomitant Medications and/or Therapies (Non-medications)

Data are collected on the following CRFs:

- Prior AEDs (Prior AED)
- Concomitant AEDs (Con AED)
- Prior and concomitant medications (MEDS)
- Prior Non-medications (Prior Non-Meds)
- Concomitant non-medications (Con Non-Med)

Rescue medications are recorded in subjects' diary, however the CRF obtains a code list of a subject's planned rescue medications. This section does not discuss details of rescue medication use.

Medication (collected on the prior/concomitant medication eCRF page) will be coded using the World Health Organization Drug Dictionary (WHO-DD).

The following algorithm will be used to define prior/baseline and concomitant medications/therapies:

Medications/therapies can be prior/baseline only, concomitant only, or prior/baseline and concomitant, depending on the start and stop dates.

- Any medication/therapy whose start and stop dates were *before* the start of study medication in Study ZX008-1503 will be considered as a prior/baseline medication.
- Any medication initiated *after* commencement of study drug in Study ZX008-1503 will be regarded as being only concomitant.
- Medications that were initiated before study drug was started in Study ZX008-1503 and ended during or after the study will be considered as *prior/baseline and concomitant*.

The medication will be assumed to be prior/baseline medication if it cannot be definitively shown that the medication did not start or continue during the OLE treatment period.

If the start date or stop date of a medication/therapy is partially missing, the date will be compared as far as possible with the date of the start of administration of study drug. The following approach will be taken:

- If the start date of medication/therapy is complete and occurs on or after the day of the first dose in 1503, the medication will be assumed concomitant only. If the start date occurs prior to the first dose date but the end date is on or after the first dose date or the medication is recorded as ongoing, the medication will be considered concomitant.
- If the start day is missing but the start month and year are complete, a medication/therapy will only be excluded as being concomitant (i.e. regarded as prior only) if the start month/year is before the month/year of study drug administration and if the stop date (either full date, month and year if missing day, or year if missing month and day) is before study drug administration.
- If the start day and month are missing but the start year is complete, a medication/therapy will only be excluded as concomitant (i.e., will be regarded as prior/baseline only) if the start year is before the year of study drug administration and if the stop date (either full date, month and year if missing day, or year if missing month and day) is before study drug administration.
- If the start date is completely missing and the stop date is prior to first dose or completely missing, the medication/therapy will be assumed a prior/baseline medication only.

Prior/baseline and concomitant medications/therapies will be summarized and sorted alphabetically, separately, by Anatomical Therapeutic Chemical (ATC) categories (Level 2: pharmacological or therapeutic subgroup and Level 3: chemical or therapeutic or pharmacological subgroup) and WHO-DD drug code. For each medication/therapy, the number and percentage of subjects will be displayed.

Summary tables will be presented on the SAF population.

All prior/baseline and concomitant medications/therapies will be listed for the safety population.

6.2.6 Prior and Concomitant Antiepileptic Treatment

Treatments (collected on the prior/concomitant antiepileptic treatment eCRF page) will be coded using the World Health Organization Drug Dictionary (WHO-DD).

Prior and concomitant antiepileptic treatments will be defined and analyzed for the SAF population similar to concomitant medications as described in section 6.2.5.

All prior and concomitant antiepileptic treatments will be listed for the SAF population.

6.2.7 Medical History

All ongoing conditions and relevant medical history from the past 5 years (including all major hospitalizations and surgeries) as well as the subject's current medical status and current medications will be carried over from the core study. AEs starting during the core study will be counted as medical history if they conclude prior to start of 1503. Ongoing AEs will be included as such in 1503.

Medical history will be summarized and sorted alphabetically, by primary System Organ Class and Preferred Term coded via the most recent version of Medical Dictionary for Regulatory Activities (MedDRA). The number and percentage of subjects will be displayed for each System Organ Class and Preferred Term within treatment group.

Medical history will be presented for the SAF population.

6.3 EFFECTIVENESS ANALYSES

All effectiveness and exploratory data will be summarized overall and by treatment group in Core study as described in Section 3.2 of this SAP. Continuous data will be summarized using descriptive statistics including means, standard deviations, medians, lower and upper quartiles, and ranges. Categorical variables will be summarized with frequencies and percentages. Point estimates and 95% confidence intervals will be calculated for key parameters as warranted. No formal comparison of treatment groups is planned.

Analyses of the key effectiveness endpoints will be performed on the mITT population, except where noted.

6.3.1 Convulsive Seizure Frequency

The key effectiveness endpoint is the change in the convulsive seizure frequency per 28 days between the pre-ZX008 Baseline and OLE Treatment Period. To aid in assessing the effect of OL treatment after treatment with blinded fixed doses, CSF per 28 days will also be presented for each pre-OLE cohort for the last weekly measure in double-blind treatment (T+M) for the entire OLE treatment period, and separately for the first, second and third months of the OLE. In addition, CSF over the remainder of the OLE treatment period will be presented, for 3-month intervals. The next section defines variables associated with these endpoints.

6.3.1.1 Variables (Estimands)

Two key CSF-related variables will be defined:

- (1) the difference in convulsive seizure frequency per 28 days (CSF) for the open-label Treatment Period (Day1 to EOS) compared to the Baseline (Core Study);
- (2) the difference in CSF for the Month2 to EOS (Day 31 to EOS) time point compared to the Baseline (Core).

Additional variables associated with the assessment of CSF are:

- Baseline (Core), Core Study (T+M), Core Study Final Week [Note: The Core Study Final Week is a subset of the Core Study (T+M) period.]

- CSF during the following time intervals: Month 1, Month 2, Month 3, Month 4-6, Month 7-9, Month 10-12, Month 13-15, Month 15-18, Month 19-21, Month 22-24, Month 25-27, Month 28-30, Month 31-33 and Month 34-36.

The frequency of convulsive seizures during a given interval will be derived from the number and type of events recorded in subject diaries. For each subject, the seizure frequency per 28 days will be calculated as the number of seizures recorded during the period, divided by the number of days in the period and multiplied by 28. The convulsive seizure frequency will be calculated from all available data collected during the relevant interval.

The Baseline (Core) convulsive seizure frequency, or CSF_{BC}, is calculated as in the Core Study using the CSF from the 42 days immediately preceding the Randomization visit in the Core Study. For any individual subject, the convulsive seizure frequency per 28 days during the baseline period (CSF_{BC}) will be derived as follows:

$$CSF_{BC} = \frac{28 \times \text{Total number of convulsive seizures during the core study baseline period}}{\text{Total number of days in the core study baseline period with nonmissing diary data}}$$

For each treatment group, the mean is obtained by averaging over the subjects in the treatment group.

The convulsive seizure frequency per 28 days for the Core Study T+M period (CSF_{CTM}) is defined below:

$$CSF_{CTM} = \frac{28 \times \text{Total number of convulsive seizures during the core study T + M period}}{\text{Total number of days in the core study T + M period with nonmissing diary data}}$$

The convulsive seizure frequency per 28 days for the Core Study Final Week of T+M (CSF_{CSFW}) is defined below:

$$CSF_{CSFW} = \frac{28 \times \text{Total number of convulsive seizures during the core study final week}}{\text{Total number of days with nonmissing diary data during the core study final week}}$$

Additionally for the other intervals (Month 1 through Month 36) defined in Table 7a, the convulsive seizure frequency per 28 days for that interval, $CSF_{OLE,\,i}$, i=1, 2, 3, … , 14, is defined as follows:

$$CSF_{OLE,\,i} = \frac{28 \times \text{Total number of convulsive seizures in the } i\text{th interval}}{\text{Total number of days in the } i\text{th interval with nonmissing diary data}}$$

The two key effectiveness measures, CSF_{E1} and CSF_{E2}, will be calculated as follows:

$$CSF_{E1} = \frac{28 \times \text{Total number of convulsive seizures from Day 1 to EOS}}{\text{Total number of days from Day 1 to EOS with nonmissing diary data}}$$

$$CSF_{E2} = \frac{28 \times \text{Total number of convulsive seizures from Day 31 to EOS}}{\text{Total number of days from Day 31 to EOS with nonmissing diary data}}$$

For each analysis group, the mean is obtained by averaging over the subjects in the analysis group.

6.3.1.2 Changes from Baseline

In all seizure analyses, the Baseline (Core) value will be the baseline used. These analyses exclude the subjects from Study ZX008-1504 Cohort 1. For any of the variables defined in the previous section, the change from baseline for any individual subject will be calculated as

$$CCSF = \text{Post-baseline value} - CSF_{BC}$$

The percentage change from baseline for any individual subject will be calculated as

$$PCCSF = (\text{Post-baseline value} - CSF_{BC}) * 100 / CSF_{BC}$$

The key effectiveness measures are CSF_{E1} and CSF_{E2}. Summary statistics for the changes from baseline and the percentage changes from baseline will also be presented. A Wilcoxon signed rank test will be used to assess the significance of the change from baseline. Given that baseline refers to the period prior to initiation of double-blind treatment in the Core study, it is expected that long-term treatment with ZX008 will lead to a reduction in convulsive seizure frequency. If we designate the mean baseline (core) CSF by μ_{BC}, and the mean for CSF_{E1} and CSF_{E2} by μ_{E1} and μ_{E2}, respectively, the key effectiveness objective is to test the null hypothesis

$$H_0: \mu_{E1} - \mu_{BC} = 0,$$

Against the alternative

$$H_A: \mu_{E1} - \mu_{BC} \neq 0,$$

Rejection of the null hypothesis in favor of the alternative, in the presence of a statistically significantly smaller mean convulsive seizure frequency during OLE Treatment (two-sided p-value < 0.05) will be regarded as evidence of a treatment benefit.

In a similar manner, each of the changes over time will be summarized and assessed for statistical significance.

The summary statistics and statistical testing will also be presented by age group.

A graph of the CSF for baseline (Core), Core Study (T+M), and during OLE Month 1 …36 will be generated, and another graph of the percentage changes from baseline may be plotted.

6.3.1.3 Treatment Group Estimates – Endpoint Analyses

The analysis of covariance (ANCOVA) analyses described in this section exclude de novo subjects. The convulsive seizure frequency per 28 days during the entire OLE Treatment period and the convulsive seizure frequency per 28 days during Month 2 to EOS, CSF_{E1} and CSF_{E2}, respectively, will each be analyzed using an ANCOVA model with age group (<6 years, ≥6 years) and treatment group (4 levels) as factors, and CSF_{BC} and CSF_{CTM} as continuous covariates. The goal of this analysis is to estimate the seizure frequency during (1) the entire OLE treatment, and (2) during Month 2 to EOS, for each of the treatment groups included in the OLE, after adjusting for the other factors in the model. To avoid taking the logarithm of 0, a value of 1 will be added

to a covariate and/or response prior to taking logs. From the general linear model, least squares estimates of treatment means and the corresponding 95% confidence intervals, will be exponentiated and a value of 1 subtracted from the result, (to offset the addition of 1 prior to taking logs), in order to provide estimates and associated 95% confidence intervals on the original scale for the response variable.

Since the ANCOVA relies on assumptions of normality, the analysis will be repeated using a nonparametric method that does not require as stringent assumptions. A nonparametric ANCOVA will be used to analyze the data, with ranks of the CSF_{BC}, and ranks of the CSF_{CTM} as covariates and ranks of the response (CSF_{E1} or CSF_{E2}); other terms/factors in the model will be the same as for the parametric ANCOVA.

Due to certain portions of the core studies remaining blinded, the ANCOVA analyses described in this section will not be submitted with the Japanese interim analysis.

6.3.1.4 Treatment Group Estimates – CSF Over Time

The general linear mixed effects model with repeated measures (i.e. MMRM) described in this section exclude de novo subjects. Analyses will be performed for the convulsive seizure frequency per 28 days, over time. In these analyses, the CSF_{CSFW} will not be included in the model. A MMRM will be employed to estimate the mean convulsive seizure frequency per 28 days, over time, for each treatment group. The model will include CSF_{BC} and CSF_{CTM} as fixed covariates; time (14 levels for Month1, Month2, Month3, Month 4-6, Month 7-9, Month 10-12, Month 12-15, Month 16-18, Month 19-21, Month 22-24, Month 25-27, Month 28-30, Month 31-33, and Month 34-36) as a fixed effect; age stratum (2 levels) as a fixed effect; treatment group (4 levels) as a fixed effect; and subject as a random effect.

CSF will be log transformed prior to analysis, and a value of 1 may be added to avoid taking the logarithm of 0.

The purpose of this modeling is to obtain least-squares adjusted means over time for the frequency of convulsive seizures per 28 days along with 95% confidence intervals.

While we seek to estimate the means over time, the variances and covariances are nuisance parameters and need to be estimated to provide associated standard errors for the treatment estimates. For the MMRM, an unstructured covariance matrix will be used. [If the model experiences convergence issues, a different covariance structure may be explored from the available choices in SAS PROC MIXED, and the covariance structure with the smallest AIC will be chosen.]

The model adjusted means and associated confidence limits will be plotted against time.

Furthermore, exploratory analysis will be carried out using a general linear model that includes the mean daily dose during OLE period (categorized as low, medium, and high) as explanatory variable, and the same factors used in the MMRM described above.

Due to certain portions of the core studies remaining blinded, the MMRM analyses described in this section will not be submitted with the Japanese interim analysis.

6.3.1.5 Seizure Frequency by Dose

Additional analyses will be performed to examine the convulsive seizure frequency over time, reported as per 28 days, by the actual dose administered.

Subjects will be grouped into low, medium, and high dose groups depending on their mean daily dose of ZX008 during the OLE Treatment period:

- Low: 0.2 to <0.4 mg/kg
- Medium: 0.4 to <0.6 mg/kg
- High: >0.6 mg/kg.

The parametric ANCOVA for the endpoint analysis will be repeated using these three dose groups in place of the four treatment groups, excluding de novo subjects.

Similarly, a nonparametric ANCOVA will be performed using these dose groups, excluding de novo subjects.

Due to certain portions of the core studies remaining blinded, the ANCOVA analyses described in this section will not be submitted with the Japanese interim analysis.

6.3.1.6 Impact of Concomitant AED Medication Use on Seizure Frequency

Subjects in the study were required to be on stable background therapy for the first 6 months of treatment, after which background AEDs could be reduced or withdrawn so long as one background AED remained. The percentage of subjects who had changes in dose or type of concomitant AED medications during the first, second, third, fourth, fifth, and sixth months will be summarized by treatment group and overall.

6.3.2 Other Effectiveness Analyses – Seizure Related

6.3.2.1 Non-convulsive Seizure Frequency per 28 Days

Similar methods as described above will be used to assess the frequency of non-convulsive seizures per 28 days.

6.3.2.2 Convulsive and Non-convulsive Seizure Frequency per 28 Days

The frequency of seizures (convulsive and non-convulsive) will be analyzed using methods similar for the analysis of convulsive seizure frequency per 28 days as described above.

6.3.2.3 Percentage of Subjects with ≥50% Reduction from Baseline

A response curve will be generated for the mITT population. This graph will plot the percentage of subjects (y-axis) against percentage reduction in seizure frequency per 28 days in the OLE treatment period (x-axis). In the graph, subjects experiencing an increase in seizure frequency will be regarded as having a 0% reduction in seizure frequency. Hence, the ordinate for time point 0 may not necessarily be at 100%. For example, if 15% of subjects have no reduction in seizure frequency between baseline and OLE Treatment period, the graph will start on the y-axis at 85%. The graph will be generated for all subjects (excluding de novo subjects), and for each age stratum and each treatment group. A separate graph will be generated for de novo subjects.

A point estimate and 95% confidence interval for the percentage of subjects achieving a ≥ 50% reduction from baseline (Core) to OLE Treatment period, and monthly periods of the OLE will be computed. This will be repeated for the Month 2 to EOS endpoint. The confidence interval for the proportion will be based on the normal approximation to the binomial distribution. The analysis will be computed for the mITT population excluding de novo subjects, and, separately, for the de novo subjects.

Similar methods will be used to estimate the proportion of subjects who achieve a 25%, reduction, 75% reduction, and 100% reduction in seizures.

6.3.2.4 Duration of the Longest Interval between Seizures

The duration of the longest interval (in days) between convulsive seizures will be analyzed.

For each subject, the longest interval between convulsive seizures will be calculated over the entire OLE period. This will be derived as the maximum of the number of days between consecutive convulsive seizures. The intervals between consecutive convulsive seizures (gaps) will be calculated as below, after which the longest interval between convulsive seizures will be derived.

If a subject has two consecutive days of missing diary data, the current seizure-free interval will be ended on the first date of missing diary data, and a new one begun on the next date that diary data are available and no seizure occurs. [In that case, for purpose of calculation of this variable, all intervening days, after the 2nd day, with missing diary data, will be assumed to have a convulsive seizure occurrence, until the first available date with non-missing diary data.]

Let Date0 (=Day1) be the first day of treatment. If convulsive seizures occur on five days having dates as Date1, Date2, Date3, Date4 and Date5, where Date5 ≥ Date4 > Date3 > Date2 > Date1 ≥ Date0, and let LDT = Last date of treatment in the OLE treatment period, where LDT ≥ Date5, then the time interval between convulsive seizures will be calculated as follows:

I1=Date2 - Date1

I2=Date3 - Date2

I3=Date4 – Date3,

I4=Date5 – Date4.

For completeness, we calculate the time to the first seizure as

I0=Date1 – Date0,

and the time from the last seizure to end of treatment as

I5 = LDT – Date5.

Here the duration of the longest interval =Maximum (I0, I1, I2, I3, I4, I5).

If the subject does not experience a seizure during treatment, then the last available diary date will be used to compute the duration of the longest interval as follows:

The longest interval=last available diary date – Date0

The median time of the longest convulsive seizure-free interval will be presented. Additional summary statistics will be presented, including mean, minimum, maximum, and the 25th and 75th percentiles, 95% confidence intervals for the percentiles using the normal approximation to the binomial distribution. Analyses will be presented for the mITT population (excluding de novo subjects), de novo mITT subjects, and all mITT subjects.

A boxplot of the duration of the longest interval (in days) between seizures will be presented. The boxplot will be presented for the mITT population (excluding de novo subjects), de novo mITT subjects, and all mITT subjects.

A summary of the recurrences of seizures and the gap times between seizures will also be presented. [The duration of the longest interval between convulsive seizures is closely related to the maximum gap time.]

6.3.2.5 The Number of Convulsive Seizure-free Days

Convulsive seizure-free days will be assessed based on the parent/caregiver diary data.

A convulsive seizure-free day will be defined as a day for which no convulsive seizures have been reported. Refer to Section 6.1.7, Missing Data. For each subject, the total number of convulsive seizure free days per 28-day period will be summed for the entire OLE Treatment period, the Month 3 to EOS period, and similarly for the baseline (Core) period.

Seizure free days per 28 days at baseline = (number of seizure free days during baseline in Core study)*28/ (number of days during baseline with non-missing diary data)

Seizure free days per 28 days during OLE Treatment Period = (number of seizure free days during OLE Treatment Period)*28/ (number of days during OLE Treatment Period with non-missing diary data)

A summary of this effectiveness endpoint will be provided over time (baseline (Core), Core Study (T+M), and OLE Month.

A MMRM will be employed with factors for subject (random effect), age group (2 levels), time, age group*time interaction as factors, and baseline (Core) and Core Study (T+M) as covariates. Least squares estimates for each age group, over time, will be obtained, along with associated 95% CIs.

Additional analysis will be done using the mean daily dose over time by grouping subjects into low, medium, and high dose groups. An MMRM will be employed, and least squares estimates of means for each age group will be obtained, along with associated 95% CIs. The MMRM will exclude de novo subjects.

6.3.2.6 Healthcare Utilization

6.3.2.6.1 Inpatient Hospitalizations Due to Seizures (All subjects)

Hospitalization data will be captured in the CRF.

Details of the hospitalizations, including reasons for hospitalization and use of resources will be summarized.

Summary statistics will include the number and percentage of subjects who experience at least one hospitalization to treat a seizure, as well as the incidence density.

6.3.2.6.2 Healthcare Utilization Questions (subjects from core study ZX008-1504 only)

In order to better understand the healthcare resource burden associated with the management of Dravet syndrome, caregivers will be asked which of the following hospital and community based healthcare services they interacted with over the preceding month: emergency room services, ambulance, planned and unplanned hospitalization, family physician services, speech and language therapy, occupational therapy, and physical therapy. This information will be captured in the CRF.

Summary statistics will include the number and percentage of subjects who utilized these services.

6.3.2.7 Incidence of Status Epilepticus Episodes

The incidence of status epilepticus during the OLE treatment period will be evaluated based on cases captured as such with treatment at hospitals or other treatment centers, those entered as adverse events (including SAEs) into the safety database, and also as convulsive seizures lasting longer than 10 min from the seizure diary. A single seizure meeting more than one of these criteria will be counted once. According to the ILAE, seizures of this duration are to be considered SE.

The number and percentage of subjects with status epilepticus recorded as an AE will be presented by treatment group and overall.

In addition, from the diary data, the number and percentage of subjects having convulsive seizures with duration >10 min during OLE will be reported by treatment group and overall.

Additionally, the number and percentage of subjects having an SE episode or a seizure with duration > 10 minutes will be summarized by treatment group and overall.

6.3.2.8 Duration of Prolonged Seizures

Duration of convulsive seizures at baseline and on treatment will be presented by treatment group and overall using categories as <2 min, 2-10 min and >10 min.

To obtain a baseline probability distribution for the three categories, we will proceed as follows: For each subject, we will calculate the percentage of their total number of baseline seizures that is in each category. (For example, if the subject had 5 seizures, with 2 in the first category and 3 in the last category, their percentage distribution would be 40%, 0%, and 60% in the <2, 2-10, and >10 categories. We can calculate similar numbers for the next subject, and so on.) We will then average these over all subjects to obtain the percentage of subjects' seizures that were <2 min in duration, the percentage between 2-10 min in duration, and the percentage >10 min in duration. These 3 percentages should total 100%. Thus, we will obtain a distribution of seizure duration for baseline.

Using the seizure duration data obtained for the OLE period, we will proceed similarly, to obtain a distribution for the OLE period.

No formal analytic method will be used to assess the distribution of seizure duration during baseline vs. during the OLE treatment period. However, it is expected that the distribution may shift in such a way that a greater proportion of seizures during the OLE period will have shorter interval duration when compared to the baseline period.

6.3.2.9 Incidence of Rescue Medication Usage

Use of rescue medication is recorded on the daily diary. In the event of prolonged seizures or status epilepticus, rescue medication is administered according to each subject's personalized regimen consisting of one or more medications. If the first rescue administration does not control the seizures, a second or even third round might be administered. The second and third round might use different medications or different doses than the first round of rescue meds.

Rescue medication will be summarized:

- The number of days rescue medication was taken (normalized to 28 days) will be summarized separately for the Baseline (Core), Month 1, Month 2, and Month 3 of the OLE Treatment Period by the mean (SD) as well as the median and range.

6.3.3 Other Effectiveness Analyses

For effectiveness rating scales administered at study visits, the overall goal is to analyze the data by visit. However, it is recognized that for a long-term study such as this, the time of the study visits might vary from pre-planned times established in the protocol. Therefore, in order to provide a common framework for the assessment of these measures, the time windows specified in Table 3 will be used. If multiple visits (scheduled or unscheduled) fall within a time window, the measurements obtained closest to the target time point will be used.

For each time point and parameter or subscale considered in these patient reported outcomes, an individual subject's value is to be obtained for the parameter and time point. The subjects' values are then the basis for obtaining treatment group means, standard deviations, etc. for the summary stats and changes form baseline.

6.3.3.1 Clinical Global Impression – Improvement Rating, as assessed by the Parent/Caregiver

The parent/caregiver will rate their global impression of the subject's condition at each visit except Visit 2.

The CGI-I scale measures the perception in the change in the subject's clinical status from a specific point in time, i.e., the Baseline Period. The CGI-I rating scale permits a global evaluation of the subject's improvement over time. The severity of a patient's condition is 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
7=very much worse

At each assessment time point during the OLE treatment period, and at End Point (End of Study or Early Termination), frequency counts (and %) of scores by severity rating will be produced overall, and by treatment group.

Descriptive statistics will be presented for the following dichotomized categories for each time point where measured, and for the last available or final (EOS/ET) assessment, and will include the number and % of subjects responding in the combined categories, along with an associated exact two-sided 95% CI.

(1) Very much improved or much improved, i.e., number of subjects with a score of 1 or 2; vs. others (3, 4, 5, 6, 7)

(2) Improved, i.e., number of subjects with a score of 1, 2, or 3; vs others (4, 5, 6, 7)

This will be presented for the mITT population as a whole, by treatment group, and for de novo subjects.

Individual subject data will be listed for CGI-I scale as assessed by the parent/caregiver.

6.3.3.2 Clinical Global Impression – Improvement Rating, as assessed by the Principal Investigator

CGI-I score data assessed by the principal investigator will be analyzed by the same methods used for CGI-I score data recorded by parent/caregiver as above.

6.3.3.3 Quality of Life in Childhood Epilepsy (QOLCE) Scale

The parent/caregiver will complete the QOLCE. This assessment evaluates how epilepsy affects day-to-day functioning of a child with epilepsy in various life areas, including physical activities, well-being, cognition, social activities, behavior and general health, at baseline period (Core study) during the OLE Treatment period, and at EOS/ET (Visit 12). There is also one question on overall quality of life, administered as part of the QOLCE.

The QOLCE scores items with a possible 5-point response. [Not including "6", "Not Applicable."] To calculate subscale scores, the 5-point item scores will first be reverse coded as necessary so that scores of 5 represent the best possible response and 1 represents the worst possible response. Item scores will then be transformed to a 0-100 scale as follows: 1 maps to 0, 2 maps to 25, 3 maps to 50, 4 maps to 75, and 5 maps to 100. After transformation, a score for each subject for each subscale is calculated by averaging that subject's responses to each item in the subscale. [A value of 0 represents the lowest or poorest score and 100 reflects the highest level of functioning.] The 16 subscale scores per subject are then averaged to obtain an overall quality of life score for each subject. The mean and standard deviation across all subjects are then calculated for each subscale, including the overall quality of life score. The higher the subscale and overall quality of life scores, the better the response.

Table 10: Subscales of the QOLCE

Domain	Subscale	Item
Section 3: Physical	Physical Restrictions	3.1 a-j
Section 3: Physical	Energy/Fatigue	3.2 a,b
Section 4: Well-being	Depression	4.1 a,d,e,l
Section 4: Well-being	Anxiety	4.1 b,g,j,n,o,p
Section 4: Well-being	Control/helplessness	4.1 c,f,h,i
Section 4: Well-being	Self-esteem	4.1 k,m,q,r,s

Domain	Subscale	Item
Section 5: Cognition	Attention/Concentration	5.1 a,d,e,f,g
Section 5: Cognition	Memory	5.1 j,k,l,m,n,o
Section 5: Cognition	Language	5.1 p,q,r,s,t,u,v,w
Section 5: Cognition	Other Cognitive	5.1 b,c,h
Section 6: Social Activities	Social Interactions	6.1 c,f,h
Section 6: Social Activities	Social Activities	6.1 a, e ; 6.2
Section 6: Social Activities	Stigma Item	6.1 i
Section 7: Behavior	Behavior	7.1 a, c,f,g,h,i,j,k,l,m,o,q,r,s,t
Section 8: General Health	General Health Item	8.1
Section 2 (USA Version) or Section 9 (Australia Version)	Quality of Life Item	2.1 or 9.1
Overall Quality of Life*		Average of 16 subscale scores*

*For each subject, an Overall Quality of Life Score will be computed by adding each subscale score for each individual and then dividing by 16.

Individual subject data for the domains will be listed.

For each subscale, descriptive statistics will be provided for the baseline, EOS/ET, and change from baseline subscale mean, overall, by treatment group and for de novo subjects.

For each treatment group at Baseline and End of Study/ET, the mean and standard deviation of the subscale score will be presented for each QOLCE subscale and for the Overall Quality of Life score.

In addition, the change from baseline in the Overall QOL score will be calculated for each subject by subtracting the baseline overall score from the overall score measured at End of Study/ET. The change from baseline for each treatment group will be summarized using the mean and standard deviation. Statistical significance of the within group change from baseline will be assessed using a Wilcoxon signed rank test.

Individual subject data for the subscales will be listed.

6.3.3.4 Quality of Life of the Parent/Caregiver using EQ-5D-5L Scale

The impact on the quality of life of the parent/caregiver responsible for a patient with DS will be assessed at Baseline (Core Study) and during the OLE Treatment period using the EQ-5D-5L.

The EQ-5D-5L health questionnaire is a health-related quality of life instrument with five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five possible levels: no problems, slight problems, moderate problems, severe problems and extreme problems.

The summary of results will follow the EQ-5D-5L guideline results presentation. For the "Health Profiles" descriptive system summary results will show the number, and percentage of subjects in each Item score (No Problems, Slight Problems, Moderate Problem, Severe Problem, Extreme Problems) overall and by treatment group, at baseline (Core), during the OLE treatment period and at EOS/ET. In addition, the item scores will be classified into two categories as "No Problems" and "Problems" comprised of items: slight, moderate, severe and extreme problems. Summary results will show number of patients and percentage with "No Problems" and with "Problems" overall, by treatment group and for de novo subjects, at baseline, during OLE Treatment period, and at EOS/ET.

In addition, the item scores will be again be classified into two categories as "Slight/No Problems" and "Moderate/Severe/Extreme Problems". Summary results will show number of patients and percentage with "Slight/No Problems" and with "Moderate/Severe/Extreme Problems" overall and by treatment group, at baseline, during OLE Treatment period, and at EOS/ET.

For the VAS measure of overall self-rated health status, descriptive statistics will be presented for the VAS absolute score and change from baseline showing number of subjects, mean, standard deviation, median, and range overall and by treatment group at baseline (Core), during OLE treatment period, and at EOS/ET. Statistical significance of the within group change from baseline will be assessed using a Wilcoxon signed ranks test.

The quality of life of parent/caregiver individual data will be listed using EQ-5D-5L scale.

6.3.3.5 Parent/Caregiver HADS Rating Scale

The HADS is a tool commonly used to determine the levels of anxiety and depression that a person is experiencing and is validated as a patient screening tool in the outpatient setting though it has not been validated specifically for caregivers. It is a 14-item scale that generates ordinal data for two dimensions: 1) Anxiety, and 2) Depression. Seven of the items relate to anxiety and seven relate to depression. Each item has four possible answers rated 0-3. All answers to the items for a dimension with their respective rating are added resulting in a range for each dimension from 0-21. Scores for the entire scale (emotional distress) range from 0 to 42, with higher scores indicating more distress.

For the Anxiety and Depression dimensions, summary descriptive statistics including the mean and SD will be generated separately for the Anxiety and Depression dimensions at each visit. In addition, for the anxiety and depression scales but not the total score, each subject will be categorized at each visit based on the score cut-offs below:

Score	Interpretation
0-7	Normal
8-10	Borderline abnormal
11-21	Abnormal

Summary statistics will include number and percentage of subjects in each of the categories above at each study visit.

In addition, the total score for Anxiety and total score for Depression will be calculated. Descriptive statistics including mean, standard deviation, median, minimum and maximum will be provided overall and for each treatment group, at baseline, during OLE treatment period and at EOS/ET. The change from baseline for each subject will be calculated by subtracting the total Anxiety and Depression score measured at Baseline from the analogous score measured at End of Study/ET. The change from baseline will be summarized by descriptive statistics as well as 95% CI for the change from baseline. A Wilcoxon signed ranks test will be used to obtain a p-value for change from baseline.

The individual item outcomes will be presented in the subject data listing.

6.3.3.6 Pediatric Quality of Life Inventory (PedsQL 4.0 Generic Core) Scale

The PedsQL 4.0 is a quality of life scale that measures four functional areas (physical, emotional, social, and school functioning). The scale is available in age-appropriate instruments with child self-report and parent proxy-report formats. In this study, the age appropriate categories for the administration of the instrument were ages 2-4, 5-7, 8-12 and 13-18 years, and the Parent Reports were used.

There are eight items for Physical Functioning (PF), and five questions each for Emotional Functioning (EF), Social Functioning (SoF), and School Functioning (ScF). Each of the responses to the 23 items is initially scored on a 5-point Likert scale from 0 (Never) to 4 (Almost always). Scores will be linearly transformed to a scale of 0 to 100, where 0=100, 1=75, 2=50, 3=25 and 4=0, and higher scores mean better health related quality of life. If more than 50% of the items in the scale are missing, the scale scores should not be computed. For each subject, a mean score is calculated for each scale (PF, EF, SoF, ScF) as the sum of the scores for items in that scale over the number of items answered. If some of the answers on a scale are missing but 50% or more of the items in the scale are completed, then impute the mean of the competed items in a scale. The scaled results will be combined across age categories to produce a single score for each functional area.

A Psychosocial Health Summary score is computed as the sum of the items over the number of items answered in the Emotional, Social, and School Functioning Scales.

A Physical Health Summary score is made up of the Physical Functioning Scale Score.

The Total Score is computed as the sum of all the items over the number of items answered on all the Scales.

Descriptive statistics for all subjects and by treatment group, at baseline, during OLE treatment period and at EOS/ET will be provided for the Psychosocial Health Summary score, the Physical Health Summary score and Total score.

The change from baseline for the Total score will be calculated for each subject by subtracting the Total score measured at Baseline from the Total score measured at End of Study/ET. The change from baseline will be summarized with descriptive statistics and the within group changes from baseline will be tested from significance from 0 using a Wilcoxon signed ranks test.

6.3.3.7 Pediatric Quality of Life Inventory (PedsQL 2.0 Family Impact Module) Scale

The PedsQL™ Family Impact Module was designed to measure the impact of pediatric chronic health conditions on parents and the family. The PedsQL™ Family Impact Module measures parent self-reported physical, emotional, social, and cognitive functioning, communication, and worry. The Module also measures parent-reported family daily activities and family relationships.

There are six items for Physical Functioning (PF), five items each for Emotional Functioning (EF), Cognitive Functioning (CF) and Worry (W), four for Social Functioning (SoF), and three for Communication (c). There are additionally three questions for Daily Activities (DA) and five for Family Relationships (FR).

Each of the responses to the 36 items is initially scored on a 5-point Likert scale from 0 (Never) to 4 (Almost always). Scores will be linearly transformed to a scale of 0 to 100, where 0=100, 1=75, 2=50, 3=25 and 4=0, and higher scores mean better health related quality of life. If more than 50% of the items in the scale are missing, the scale scores should not be computed. For each subject a mean scale score is calculated for each scale (PF, EF, CF, W, SoF, C, DA, FR) as the sum of the scores for items in that scale over the number of

items answered. If some of the answers on a scale are missing but 50% or more of the items in the scale are completed, then impute the mean of the competed items in a scale.

The Parent HRQL Summary Score (20 items) is computed as the sum of the items divided by the number of items answered in the Physical, Emotional, Social, and Cognitive Functioning scales.

The Family Functioning Summary Score (8 items) is computed as the sum of the items divided by the number of items answered in the Daily Activities and Family Relationships scales.

The Total Score is the sum of all 36 items divided by the number of items answered.

Descriptive statistics for baseline and EOS/ET will be provided for the summary scores. The change between baseline and EOS/ET in the Summary Scores and Total score will be assessed for significance using a Wilcoxon signed-rank test.

6.3.3.8 Study Medication Palatability Assessment

The palatability and acceptability of the IMP will be assessed indirectly by the parent/caregiver responsible for the patient according to the schedule in Table 1 using three questions:

QUESTION 1: Over the past month, on the basis of the reaction/facial expression of your child, do you think that the medicine's taste and texture are:

- Acceptable to your child
- Not acceptable to your child

QUESTION 2: Over the past month, please rate how much your child likes/dislikes the medicine's taste using the following grading scale:

- 5 (likes it very much)
- 4 (likes it)
- 3 (neither likes it or dislikes)
- 2 (dislikes it)
- 1 (dislikes it very much)

QUESTION 3: Over the past month, do you sometimes have problems giving the medicine to your child due to its taste or texture?

- No
- Yes
    - How often?
        - Every day in the past month
        - Once to several times every week in the past month
        - Once or several times in the past month

Palatability will be assessed through descriptive statistical methods. For example, the percentage of parents or caregivers who consider the medicine's taste and texture to be acceptable to the child will be presented along with a 95% CI at each time point data are available.

6.3.4 Exploratory Analysis (in subjects from core study ZX008-1504 only)

The following exploratory effectiveness endpoints will be assessed for subjects from ZX008-1504 from whom these data are obtained.

6.3.4.1 Sleep Quality and Mealtime Behavior Questions

The parent/caregiver will be asked to indicate the appropriate response that adequately describes their child's sleep quality and eating behavior since starting IMP based on the following questions:

1. Since your child has started taking the study medication in this study, have you noticed that s/he has been waking in the middle of the night or very early in the morning more than usual?
    - My child's sleep is more disturbed than it was before s/he started the study medication
    - My child's sleep patterns are the same as they were before starting the study medication
    - My child sleeps better than s/he did before starting the study medication
2. Since your child has started taking the study medication in this study, have you noticed that s/he has had a change in their mealtime behavior?
    - My child has worse mealtime behavior since starting the study medication
    - My child's mealtime behavior has not changed since starting the study medication
    - My child has improved his/her mealtime behavior since starting the study medication

The responses will be summarized using counts and percentages.

6.3.4.2 Karolinska Sleepiness Scale

The Karolinska Sleepiness Scale will be administered according to the schedule in Table 1. The Karolinska Sleepiness scale is a self-report scale that measures the subject's drowsiness. It is a 9-point verbally anchored scale, which ranges from 'extremely alert' at one end of the scale to 'extremely sleepy – fighting sleep' at the other end of the scale. Within this study, the scale will be completed by the observer. The scale scores (responses) are as follows:

Table 11: Karolinska Sleepiness Scale Score Description

[redacted]

[redacted]

Scores of 1-6 may be categorized as “active” and scores of 7-9 may be categorized as “sleepy”.

Assessments will be made at Visit1 (Baseline), and each visit from Visit 3 through Visit 16.

The categories will be summarized using counts and percentages for each time point.

The scores will be summarized using mean, standard deviation, median, minimum and maximum, for baseline and time point.

6.4 SAFETY ANALYSIS

Safety will be assessed through evaluation of AEs, Laboratory data (hematology, chemistry, urinalysis), vital signs (blood pressure, heart rate, temperature, and respiratory rate), Physical examination, Neurological examination, 12-lead ECGs, Doppler ECHOs, Tanner Staging, BRIEF to measure cognition, and Columbia–Suicide Severity Rating Scale.

All safety analyses will be performed for the SAF population and will be reported for all subjects overall. Select analyses may be repeated by treatment group, for example, treatment-emergent adverse events initiating on or before Visit 2 (Week 2), Visit 3 (Month 1), and Visit 4 (Month 2).

6.4.1 Adverse Events

An AE is 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. The period of observation for adverse events extends from the time the subject gives informed consent until 15 days after the last dose of study drug or the last visit, whichever is later. For patients who continue into the open-label extension study, AEs from the core studies will be considered medical history unless there is an increase in the frequency or severity of the condition from the core study.

A TEAE is defined as any AE that based on start date information occurs after the first intake of study treatment. All other AEs occurring after enrollment and prior to the first administration of study treatment are defined as non-treatment emergent AEs (non-TEAEs).

AEs are categorized as related or not related to IMP. Per protocol, the following rule was used to assess causality of an AE to IMP:

- Not Related: Concomitant illness, accident or event with no reasonable association with study drug.
- Related: The event follows a reasonable temporal sequence from administration of study drug and is definitive pharmacologically; cannot to be attributed to concurrent disease or other factors or medications. A clinically reasonable response should be observed if the study drug is withdrawn or dose reduced.

Any missing relationship/causality assessment will be considered as “related.”

The severity of AEs (whether non-serious or serious) will be assessed by the investigator as follows:

- Mild - A type of AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living.
- Moderate - A type of AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research participant.
- Severe - A type of AE that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.

Per the CDISC SDTM Severity Intensity Scale for Adverse Event Terminology, any missing severity will be imputed as "severe."

The original terms used by the investigators in the eCRFs to identify AEs will be coded using the most recent version of the MedDRA implemented by the sponsor at the end of the study.

6.4.1.1 Overview of Adverse Events:

The number and percent of patients with at least one of the following events will be summarized in an overall summary table:

- TEAE
- Serious TEAE
- Related TEAE
- Related serious TEAE
- Severe TEAEs
- Adverse events of special interest
- Deaths

The percentage denominator for the calculation of percentage will be the number of subjects in the SAF population. The above summary will be provided for the OLE treatment period.

6.4.1.2 Treatment Emergent Adverse Events

The following summaries will display the number and percentage of subjects with an adverse event as well as the corresponding number of events by system organ class (SOC) and preferred term (sorted alphabetically):

- All TEAEs
- All TEAEs occurring in ≥5% of subjects
- Serious TEAEs
- TEAEs by Maximum Severity
- TEAEs by prior treatment group, with onset before or up to Visit 1, Visit 2; Visit 3; Visit 4
- Study Drug Related TEAEs

- Study Drug Related TEAEs occurring in ≥5% of subjects
- All AEs that lead to premature discontinuation from the study

No inferential statistical methods (i.e., methods that yield p-values) will be used to compare treatment groups on the frequency or severity of AEs.

These summaries will be provided for the OLE treatment period.

Additionally, the following listings will be produced for all enrolled subjects:

- All AEs, events considered to be TEAE will be identified in the listing
- Serious AEs
- AEs that lead to premature discontinuation from the study

6.4.2 Adverse Events of Special Interest (AESI)

As per ICH guidance (E2F Development Safety Update Report [2011]), the Sponsor has identified the following AESIs for the ZX008 program.

Table 12 Adverse Events of Special Interest:

Metabolic/Endocrine
1. Elevated prolactin level ≥ 2x above the upper limit of normal (ULN)
2. Hypoglycemia – serum blood glucose more than 20% below the glucose level on Study Day -1 value or more than 10% below LLN (reference range 60 – 140 mg/dL)
Neuropsychiatric
1. Suicidal thoughts, ideation or gestures

LLN = lower limit of normal; ULN = upper limit of normal

The following summary tabulations will be provided to explore the AEs of special interest:

- AEs with decreased appetite or hypophagia

Adverse events of special interest will be summarized overall, and by treatment group, ZX008 combined and overall by system organ class and preferred term for the OLE treatment period.

All adverse events of special interest will be listed separately.

6.4.3 Physical Examination

A complete physical examination will be performed at Visit 1 and EOS/ET visit (Visit 16), and at the Cardiac follow-up visits (Visit 17 and 18). An abbreviated physical exam is performed at Day 15 (Visit 2), Visit 3 through Visit 16 (Days 30, 60, 90, 180, 270, 365, 455, 545, 635, 725, 815, 905 and 995)

All physical examination results will be presented in a subject data listing, including the description of abnormalities.

6.4.4 Neurological Examination

A complete neurological examination will be performed at baseline (OLE) Visit (Visit 1) and at EOS / ET (Visit 16).

All neurological examination results will be presented in a subject data listing, including the description of abnormalities.

6.4.5 Vital Signs, Weight, and BMI

Vital signs data including blood pressure, heart rate, temperature, respiratory rate, weight, and BMI will be documented for subjects during study Visits 1 through Visit 16 (EOS/ET).

The actual value and change from baseline (OLE) to each on-study evaluation time point will be summarized for vital signs and weight overall and by treatment group. Vital signs, weight and BMI data will be presented for each patient in a data listing.

A listing of subjects with Potentially Clinical Significant vital sign results will be provided. In this listing, those values outside the sponsor defined alert ranges will be marked and further available details about clinical relevance and diagnosis will be added.

Descriptive statistics will be provided for weight over time at baseline (OLE), and every 3 months during the OLE treatment period, for all subjects in the safety population. For the same time periods, the percent of subjects who lost at least 7% or 10% of their body weight during OLE when compared to baseline (OLE) will be summarized. Similarly, the percent of subjects who gained 7% or 10% of their body weight during OLE when compared to baseline (OLE) will be summarized. For subjects who lost at least 7% of their body weight, the number who achieved a recovery to their baseline (OLE) weight, and the duration of time to recovery, will be summarized. Recovery will be defined as achieving a weight, after the ≥ 7% reduction, which is at least 99% of the baseline (OLE) weight at two separate, consecutive assessments. The number of days until weight recovery will be determined using the date of the first date where the weight loss was observed and the first date where the subject's weight had recovered to, and maintained for at least two consecutive study visits, at least 99% of the baseline (OLE) weight. A similar analysis of 5% weight loss and weight gain will be conducted.

In addition, weight will be summarized by age group (2-<4; 4-<6; 6 to<12; and ≥12 years).

A scatterplot will plot height and age for subjects at the end of the OLE period.

6.4.6 Electrocardiogram

12-Lead ECGs data will be obtained during study at baseline (Core study), baseline (OLE), Visit 1, and Visit 3 through Visit 16 (End of Study/ET) and at Cardiac Follow-up (Visits 17 and 18).

A separate report will be provided by the ECG vendor.

6.4.7 Doppler Echocardiography

Doppler echocardiography will be conducted at a facility with experience for the subject's age at baseline (Core study), baseline (OLE), Visit 1, and Visit 3 through Visit 11, at End of Study/ET (Visit 16) and at Cardiac Follow-up (Visits 17 and 18).

A separate report will be provided by the ECHO vendor.

6.4.8 Tanner Staging

Tanner Staging will be assessed for subjects >7 years old during the study at baseline (Core) period, baseline (OLE), and at Visit 3 through Visit 15 and EOS/ET (Visit 16). Conceptually, pubertal maturation can be described in terms of sequence, timing, and tempo. Puberty consists of a series of predictable events, and the sequence of changes in secondary sexual characteristics has been categorized by several groups. The onset and progress of pubertal changes will be recorded on a 5-point scale for boys and girls separately. Boys are rated for genital development and pubic hair growth through stage I to stage V. Girls are rated for breast development and pubic hair growth through stage I to stage V.

The number and percentage of subjects in each Tanner Stage will be presented for baseline (Core) and EOS by treatment group separately for boys and girls.

All Tanner staging data will be presented in the subject data listing.

6.4.9 Laboratory Parameters

Blood samples for clinical laboratory evaluation will be obtained at each study visit as indicated in the schedule of assessments given in Table 1. Laboratory safety parameters will be analyzed by a central laboratory using standard validated methods.

The following continuous laboratory parameters will be analyzed:

- Hematology: hemoglobin, hematocrit, erythrocytes, erythrocyte mean corpuscular volume, leukocytes, neutrophils, lymphocytes, monocytes, eosinophils, basophils and platelets
- Blood Biochemistry: albumin (ALB), alkaline phosphatase (AP), alanine aminotransferase (ALT; SGPT), aspartate aminotransferase (AST; SGOT), blood urea nitrogen (BUN), calcium (Ca), carbon dioxide (CO2), chloride (Cl), creatinine, creatine kinase, gamma-glutamyl transferase (GGT), globulin, glucose, lactate dehydrogenase (LDH), phosphorus, potassium (K), sodium (Na), thyroid function, thyroid stimulating hormone (TSH), total bilirubin, direct bilirubin, total cholesterol, total protein, triglycerides, uric acid.
- Tests of growth and precocious puberty: Growth hormone (GH), insulin-like growth factor-1 (IGF-1, low sensitivity), prolactin, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), testosterone, estradiol
- Epilepsy genotype panel
- Coagulation: Prothrombin time (PT)/International normalized ratio (INR), activated partial thromboplastin time (PTT)
- Whole blood cannabidiol
- Urinalysis: analysis for pH, glucose, ketones, nitrite, protein, bilirubin, urobilinogen, leukocyte esterase, and occult blood. Microscopic analysis will be performed for blood, all cell types, and casts.

- Urine pregnancy test: Urine pregnancy testing will be performed in female subjects of childbearing potential.
- Urine THC panel

Observed continuous laboratory data will be descriptively summarized by type of laboratory test/parameter overall and by treatment group. Changes from baseline will also be presented for all continuous laboratory parameters overall and by treatment group over time.

Categorical laboratory parameters will be summarized by presenting the number and percentage of subjects by visit for all subjects and by treatment group.

All laboratory values (including invalid values, reference ranges, and possible flags (low, high,)) will be presented in the subject data listings.

A listing of subjects with extreme laboratory results will be provided.

6.4.10 Columbia-Suicide Severity Rating Scale

The Columbia–Suicide Severity Rating Scale (C-SSRS) is an assessment tool that evaluates suicidal ideation (including intent), and behavior. Baseline (core study) data were collected in the screening visit (Visit 1) of the Core study using the C-SSRS Children's Baseline/Screening Assessment. For the current study, baseline (OLE) Treatment period data and Visits 3 through Visit 15 and EOS/ET (Visit 16) data are collected using the C-SSRS Children's 'Since Last Visit Assessment.

Subjects who are younger than 7 years chronologically, or who are judged by the investigator not to have the mental capacity to understand the questions as specified on the C-SSRS, will not complete the rating. The investigator should use his/her judgment to substitute intellectually appropriate questions to probe the tendency for self-harm.

If a subject with the intellectual capacity to complete the C-SSRS reaches 7 years of age during the study, use of the C-SSRS should be initiated at subsequent visits.

6.4.10.1 Suicidal Ideation

The following outcomes are C-SSRS categories and have binary responses (yes/no):

[redacted]

Suicidal ideation is assessed as a "yes" answer at any time during the OLE treatment period to any one of the five questions (1-5) above. The number and percentage of subjects with suicidal ideation will be presented, as well as the number and percentage having a "yes" response to each category (1-5) at least once during the OLE period. The denominator will be the number of subjects completing the C-SSRS at least once during the OLE treatment period.

6.4.10.2 Suicidal Behavior

The following outcomes are C-SSRS categories and have binary responses (yes/no):

Suicidal behavior is assessed as a "yes" answer at any time during the OLE treatment period to any one of the five questions (6-10) above. The number and percentage of subjects who had suicidal behavior, as well as the number and percentage having a "yes" response to each category (6-10) at least once during the OLE period. The denominator will be the number of subjects completing the C-SSRS at least once during the OLE treatment period.

6.4.10.3 Suicidal Ideation or Behavior

An overall composite will be provided similar to the suicidal ideation and behavior composite endpoints but will instead count a subject if any of the C-SSRS questions 1 through 10 is marked as "yes" any time during the OLE period.

6.4.10.4 Self-injurious Behavior without Suicidal Intent

Self-injurious behavior without suicidal intent is also a C-SSRS outcome (although not suicide related) and has a binary response (yes/no).

The number and percentage of subjects having reported anytime during the OLE treatment period experiencing a 'Self-injurious behavior without suicidal intent' event (Question 11) will be provided.

6.4.11 Brief Rating Inventory of Executive Function (BRIEF, BRIEF-P, BRIEF-A)

The Behavior Rating Inventory of Executive Function (BRIEF™) , preschool version, BRIEF-P, and adult version (used for subjects aged 19-35), are standardized, validated rating scales to measure executive function in children within the home and school environments that will be assessed by the parent according to the schedule in Table 1.

The BRIEF measures multiple aspects of executive functioning; scales include Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials and Monitor.

The original BRIEF was the basis for the development of the BRIEF-P. The BRIEF-P Rating Form consists of 63 items that measure various aspects of executive functioning: Inhibit Shift, Emotional Control, Working Memory, and Plan/Organize.

The BRIEF-A Rating Form consists of 75 items that measure various aspects of executive functioning. Nine overlapping scales are created.in two different indexes. For the BRIEF-A, the BRI is composed of four scales: Inhibit, Shift, Emotional Control, and Self-Monitor. The Metacognition Index is composed of five scales: Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials. The BRI and MI combine to yield the GEC Index.

For the BRIEF, BRIEF-P, and BRIEF-A, mean scores at Baseline, End of Study/ET and mean change from baseline to End of Study/ET, and descriptive statistics will be presented by treatment group and overall for the Safety population (SAF).

6.5 PK/PD ANALYSIS

Not applicable.

6.6 ANALYSIS OF OTHER ASSESSMENTS

Not applicable

6.7 INTERIM ANALYSIS

Accumulating safety data from this study may be provided to and be reviewed by the Sponsor and its representatives and/or to an Independent Data and Safety Monitoring Committee (IDSMC) or regulatory authority as needed in order to fulfill regulatory requirements.

A planned interim analysis was conducted to support product registration. All subjects who had enrolled in the study on or before March 13, 2018 were included in the analysis. The data cutoff for the interim analysis was April 27, 2018. All CRF and vendor data obtained on or before April 27, 2018 were included, and electronic diary data obtained up to June 18, 2018, for subjects enrolled on or before March 13, 2018, were included.

The specific list of TFLs that were presented in the interim analysis were delineated in the Table of Contents for the TFL shells.

Additionally, data on all subjects were included in the Integrated Summary of Effectiveness and the Integrated Summary of safety for the ZX008 NDA. Within the ISS and ISE, data presentations for subjects from Study 1 and Study ZX008-1504 Cohort 2 were designated by their double-blind treatment regimens since those data had been unblinded at the time of the NDA submission.

An interim cut and analysis of subjects enrolled from Japan will be completed after all subjects from Japan have reached the 3 Month time point in the study. The specific list of TFLs that will be presented in the interim analysis are delineated in the Table of Contents for the TFL shells.

A final analysis and report of all data obtained from this study will be provided within 6 months of completion of the last subject's final study visit.

6.8 INDEPENDENT DATA AND SAFETY MONITORING COMMITTEE

The IDSMC is an independent advisory body that monitors participant safety, data quality and progress of the clinical trial. The IDSMC charter will outline the roles and responsibilities of the committee and guide its operations and frequency of meetings. The IDSMC will consist of individuals external to the sponsor who have relevant clinical trial expertise and experience in safety assessment.

At regularly defined intervals, the IDSMC will convene to review and monitor study progress, AEs and SAEs, other measures of safety such as ECGs or ECHOs, and efficacy data as dictated by the charter.

The IDSMC will:

- Be responsible for providing recommendations to the sponsor surrounding study conduct matters that affect safety.
- Review safety data at ad hoc time points and identify if significant safety concerns arise during the study.
- Review pharmacokinetic data and any other data that may affect subject continuation.
- Make recommendations regarding the continuation, suspension, or termination of the study.

Tables, listings, and figures will be provided to the IDSMC as per IDSMC charter.

6.9 INTERNATIONAL PEDIATRIC CARDIAC ADVISORY BOARD (IPCAB)

The IPCAB is an advisory body to the sponsor that monitors cardiac safety of the ZX008 clinical trials and provides advice to the IDMSC. The IPCAB charter outlines the roles and responsibilities of the committee and guide its operations, and review of individual subject cases. The IPCAB consists of individuals external to the sponsor who have relevant experience in cardiology, pediatric cardiology, and echocardiography. The IPCAB will advise the sponsor and the IDMSC on the cardiac safety-monitoring plan, including alert criteria and decision pathway for subject management relative to cardiac safety in the clinical studies of ZX008.

All ECHO examinations performed throughout the trial will be sent to an experienced pediatric cardiologist central reader (Biomedical Systems, Inc.). If the central reader classifies a subject as having met a pre-defined threshold value indicative of potential cardiac valvulopathy or pulmonary hypertension, or any other unexpected cardiac adverse event, the case will then be sent for secondary adjudication by one or more members of the IPCAB according to the procedures outlined in the IPCAB manual. In addition, member of the IPCAB will perform audits of ECHOs deemed normal by the central cardiac reader.

6.10 CHANGES TO METHODS PLANNED IN THE PROTOCOL

There were no changes in this SAP when comparing to the protocol are specified below.

7. REFERENCES

Dravet C, Bureau M, Oguni H, Fukuyama Y, Cokar O. Severe myoclonic epilepsy in infancy: Dravet syndrome. Adv Neurol 2005; 95: 71-102.

Dravet C. Les epilepsies graves de l'enfant. Vie Med. 1978; 8:543–548.

Dravet C. Severe myoclonic epilepsy in infants and its related syndromes. Epilepsia 2000; 41:7.

EMA 2007. Stiripentol SmPC and EPAR Scientific Discussion. Available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000664/human_med_000742.jsp&mid=WC0b01ac058001d124. Accessed 31 July 2015.

Hurst, DL. Epidemiology of severe myoclonic epilepsy of infancy. Epilepsia 1990; 31:397-400.

ICH Topic E2F: Development Safety Update Report, 2011.

Sabaz M, Carins D, Lawson J, Nheu N et al. Validation of a New Quality of Life Measure for Children with Epilepsy. Epilepsia 2000; 41(6):765-774.

Sabaz M, Carins D, Lawson J, Nheu N et al. The health-related quality of life of children with refractory Epilepsy: A comparison of those with and without intellectual disability 2001; 42(5):621-628.

Shorvon S, Tomson T. Sudden unexpected death in epilepsy. Lancet 2011;378: 2028–38.

Talarska D. The usefulness of Quality of Life Childhood Epilepsy (QOLCE) questionnaire in evaluating the quality of life of children with epilepsy. Advances Med. Sci 2007; 52 suppl 1:191-193.

8. APPENDICES

APPENDIX 1: LIST OF PLANNED TABLES, FIGURES AND LISTINGS FOR FINAL REPORT

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
	14.1	**Subject Information**			
	14.1.1	**Subject disposition, protocol deviations, and study populations**			
Table	14.1.1.1	Subject disposition – all enrolled subjects	Y	Y	
Table	14.1.1.1.1	Subject disposition – all enrolled subjects (Japan)			Y
Table	14.1.1.2	Major protocol deviations – Safety Population	Y	Y	
Table	14.1.1.2.1	Major protocol deviations – Safety Population (Japan)			Y
Table	14.1.1.3	Study Populations	Y		
Table	14.1.1.3.1	Study Populations (Japan)			Y
	14.1.2	**Demographic and baseline characteristics**			
Table	14.1.2.1	Demographic and baseline Characteristics – Safety Population	Y	Y	
Table	14.1.2.1.1	Demographic and baseline Characteristics – Safety Population (Japan)			Y
Table	14.1.2.2	Demographic and baseline Characteristics – mITT Population	Y		
Table	14.1.2.2.1	Demographic and baseline Characteristics – mITT Population (Japan)			Y
	14.1.3	**Medical history**			
Table	14.1.3.1	Medical history – Safety Population			
Table	14.1.3.1.1	Medical history – Safety Population (Japan)			Y
	14.1.4	**Prior/Baseline and concomitant medications and therapies/treatments**			
Table	14.1.4.1	Prior/Baseline medications and therapies/treatments – Safety Population			
Table	14.1.4.2	Concomitant medications and therapies/treatments – Safety Population			
Table	14.1.4.3	Prior/Baseline antiepileptic treatment – Safety Population		Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.1.4.3.1	Prior/Baseline antiepileptic treatment – Safety Population (Japan)			Y
Table	14.1.4.4.1	Concomitant antiepileptic treatment – Safety Population	Y	Y	
Table	14.1.4.4.1.1	Concomitant antiepileptic treatment – Safety Population (Japan)			Y
Table	14.1.4.4.2	Frequency Distribution for Number of Concomitant Antiepileptic Treatments-Safety Population	Y		
Table	14.1.4.4.2.1	Frequency Distribution for Number of Concomitant Antiepileptic Treatments-Safety Population (Japan)			Y
	14.1.5	**Treatment Exposure and compliance**			
Table	14.1.5.1	Duration of Treatment Exposure – Safety Population	Y	Y	
Table	14.1.5.1.1	Duration of Treatment Exposure by Age Group – Safety Population		Y	
Table	14.1.5.1.2	Duration of Treatment Exposure by Sex – Safety Population		Y	
Table	14.1.5.1.3	Duration of Treatment Exposure – Safety Population (Japan)			Y
Table	14.1.5.1.4	Duration of Treatment Exposure by Age Group – Safety Population (Japan)			Y
Table	14.1.5.1.5	Duration of Treatment Exposure by Sex – Safety Population (Japan)			Y
Table	14.1.5.1.6	Duration of Treatment Exposure in ZX008-1502 and ZX008-1503 Combined (Subjects Treated in ZX008-1502 or ZX008-1503) (Japan)			Y
Table	14.1.5.1.7.1	Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit – Safety Population			
Table	14.1.5.1.7.2	Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit – Safety Population (Japan)			Y
Table	14.1.5.1.8.1	Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment – Safety Population			
Table	14.1.5.1.8.2	Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment – Safety Population (Japan)			Y
Table	14.1.5.1.9.1	Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment – Safety Population			
Table	14.1.5.1.9.2	Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment – Safety Population (Japan)			Y
Table	14.1.5.1.10.1	Number of Subjects Receiving ZX008 According to Actual Dose (mg/kg) and Duration of Treatment – Safety Population			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.1.5.1.10.2	Number of Subjects Receiving ZX008 According to Actual Dose (mg/kg) and Duration of Treatment – Safety Population (Japan)			Y
Table	14.1.5.2.1	Compliance to IMP intake – Safety Population	Y	Y	
Table	14.1.5.2.1.1	Compliance to IMP intake – Safety Population (Japan)			Y
Table	14.1.5.2.2	Compliance to IMP intake – mITT Population	Y	Y	
Table	14.1.5.2.2.1	Compliance to IMP intake – mITT Population (Japan)			Y
	14.2	**Effectiveness**			
	14.2.1	**Effectiveness – Convulsive Seizure Frequency**			
Table	14.2.1.1.1	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics and Tests of Changes from Baseline	Y	Y	
Table	14.2.1.1.2	Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group: Summary statistics and Tests of Changes from Baseline – mITT Population	Y		
Table	14.2.1.1.3	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary Statistics and Tests of Changes from Baseline –mITT Population	Y		
Table	14.2.1.1.4	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, , by Age Group: Summary Statistics and Tests of Changes from Baseline – mITT Population	Y		
Table	14.2.1.1.5	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics – 1504 Cohort 1 Subjects	Y		
Table	14.2.1.1.6	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.1.7	Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group: Summary Statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.1.8	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary statistics and Tests of Changes from Baseline –mITT Population (Japan)			Y
Table	14.2.1.1.9	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, by Age Group: Summary statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.2	Convulsive seizure frequency per 28 days - Endpoint: Parametric analysis – mITT Population			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.2.1.3	Convulsive seizure frequency per 28 days - Endpoint: Nonparametric analysis – mITT Population			
Table	14.2.1.4	Convulsive seizure frequency per 28 days, Over Time - Parametric analysis – mITT Population			
Table	14.2.1.5	Convulsive seizure frequency per 28 days, Over Time, Using Mean Daily Dose: Parametric Analysis – mITT Population			
Table	14.2.1.6	% of subjects with Changes in AED medications during the first 6 months of the OLE Treatment Period – mITT Population			
Figure	14.2.1.7	Graph of means for convulsive seizure frequency per 28 days - mITT Population			
Figure	14.2.1.8	Graph of model adjusted means for Convulsive seizure frequency per 28 days – mITT Population			
Figure	14.2.1.9	Graph of convulsive frequency per 28 days, Over Time, Using Mean Daily Dose – mITT Population			
	14.2.2	**Effectiveness – Proportion of responders for convulsive seizure frequency**			
Table	14.2.2.1	Percent reduction in convulsive seizure frequency, OLE Treatment Period– mITT population	Y	Y	
Table	14.2.2.1.1	Percent reduction in convulsive seizure frequency, OLE Treatment Period– mITT population (Japan)			Y
Figure	14.2.2.2	Cumulative response curves for percent reduction in CSF during OLE Treatment Period – mITT population	Y	Y	
Figure	14.2.2.2.1	Cumulative response curves for percent reduction in CSF during OLE Treatment Period – mITT population			Y
	14.2.3	**Effectiveness – Duration of Longest interval between convulsive seizures**			
Table	14.2.3.1	Duration of Longest interval between convulsive seizures during OLE Treatment Period – mITT Population			
Figure	14.2.3.2	Boxplot of distribution of duration of longest interval between convulsive seizures during OLE Treatment Period – mITT Population			
	14.2.4	**Effectiveness – Summary of duration of convulsive episodes**			
Table	14.2.4.1	Summary of Duration of Convulsive Seizure Episodes during OLE Treatment Period - mITT Population			
Table	14.2.4.2	Summary of Gaps between Convulsive Seizure Episodes during OLE Treatment Period mITT Population			
	14.2.5	**Effectiveness – Number of convulsive seizure free days**			
Table	14.2.5.1	Convulsive seizure-free days – summary statistics – mITT Population			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.2.5.2	Convulsive seizure-free days – Parametric Analysis by Age Group - mITT Population			
Table	14.2.5.3	Convulsive seizure-free days – Parametric Analysis by Mean Daily Dose - mITT Population			
Table	14.2.5.4	Convulsive seizure-free days – summary statistics for subjects from Study 1504 –Cohort 1			
	14.2.6	**Effectiveness –non-convulsive and convulsive seizure frequency**			
Table	14.2.6.1	Non-convulsive seizure frequency during OLE Treatment Period – mITT Population			
Table	14.2.6.2	Convulsive + non-convulsive seizure frequency during OLE Treatment Period – mITT Population			
	14.2.7	**Effectiveness – Incidence of rescue medication**			
Table	14.2.7.1	Days with Rescue medication usage during OLE Treatment Period – mITT Population	Y		
Table	14.2.7.2	Days with Rescue medication usage during OLE Treatment Period – mITT Population (Japan)			Y
	14.2.8	**Effectiveness – Incidence of hospitalization to treat seizure**			
Table	14.2.8.1	Hospitalization and Other Healthcare Resource Utilization to Treat Seizure - mITT Population– mITT Population			
Table	14.2.8.2	Hospitalization and Other Healthcare Resource Utilization to Treat Seizure - mITT Population– mITT Population (Japan)			**Y**
	14.2.9	**Effectiveness – Incidence of status epilepticus**			
Table	14.2.9.1	Number of episodes of status epilepticus during OLE Treatment Period - mITT Population			
Table	14.2.9.1.1	Number of episodes of status epilepticus during OLE Treatment Period - mITT Population (Japan)			Y
Table	14.2.9.2	Duration of Seizures – mITT Population			
	14.2.10	**Effectiveness – Clinical Global Impression** of Improvement, **– Rating by Parent/Caregiver and Investigator**			
Table	14.2.10.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population	Y		
Table	14.2.10.1.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population (Japan)			Y
Figure	14.2.10.2	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population	Y		
Figure	14.2.10.2.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.2.10.3	Clinical Global Impression of Improvement, Investigator Rating – mITT Population	Y		
Table	14.2.10.3.1	Clinical Global Impression of Improvement, Investigator Rating – mITT Population (Japan)			Y
Figure	14.2.10.4	Clinical Global Impression of Improvement, Investigator Rating – mITT Population	Y		
Figure	14.2.10.4.1	Clinical Global Impression of Improvement, Investigator Rating – mITT Population (Japan)			Y
	14.2.11	**Effectiveness – Quality of Life in Childhood Epilepsy Scale**			
Table	14.2.11.1	Quality of Life in Childhood Epilepsy (QOLCE) – mITT population			
	14.2.12	**Effectiveness – Peds QL**			
Table	14.2.12.1	PedsQL Pediatric Quality of Life Inventory (Version 4.0) - Parent Report – mITT Population			
Table	14.2.12.2	PedsQL Family Impact Module (Version 2.0) – Parent Report – mITT Population			
	14.2.13	**Effectiveness –Quality of Life of the Parent /Caregiver using EQ-5D-5L Sale**			
Table	14.2.13.1	QOL of Parent/Caregiver using EQ-5D-5L –QOL of Parent/Caregiver Based on EQ-5D-5L: Health Profile Summary Original Response Categories – mITT Population			
Table	14.2.13.2	QOL of Parent/Caregiver Based on EQ-5D-5L: Health Profile Summary Using Dichotomized Response Categories – mITT Population			
Table	14.2.13.3	QOL of Parent/Caregiver Based on EQ-5D-5L: Overall Health Status Using VAS (0-100) Scale - mITT Population			
	14.2.14	**Effectiveness –Quality of Life of the Parent /Caregiver using HADS Scale**			
Table	14.2.14.1	Parent/Caregiver Ratings Based on Hospital Anxiety and Depression Scale (HADS): Normal; Borderline Abnormal; and Abnormal Categories – mITT population			
Table	14.2.14.2	Parent/Caregiver ratings Based on Hospital Anxiety and Depression Scale (HADS): Total Score – mITT population			
	14.2.15	**Exploratory objectives (feeder study ZX008-1504 subjects only)**			
Table	14.2.15.1	Study medication palatability assessment	Y		
Table	14.2.15.2	Sleep quality and mealtime behavior – mITT population			
Table	14.2.15.3	Karolinska sleepiness scale – mITT population			
	14.3	**Safety**			
	14.3.1	**Summary of adverse events**			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.1	Overview of number of subjects with TEAE during OLE Treatment Period – Safety Population	Y	Y	
Table	14.3.1.1.1	Overview of number of subjects with TEAE during OLE Treatment Period – Safety Population (Japan)			Y
Table	14.3.1.2.1	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Population	Y	Y	
Table	14.3.1.2.1.1	Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (< 6 yrs, ≥6 yrs) by MedDRA System Organ Class and Preferred Term – Safety Population		Y	
Table	14.3.1.2.1.2	Treatment-Emergent Adverse Events with Decreased Appetite, Loss of appetite, or Hypophagia during Open-Label Treatment Periods – Safety Population		Y	
Table	14.3.1.2.2	Treatment-Emergent Adverse Events occurring in ≥5% of subjects by MedDRA System Organ Class and Preferred Term– Safety population	Y	Y	
Table	14.3.1.2.2.1	Treatment-Emergent Adverse Events occurring in ≥5% of subjects by MedDRA System Organ Class and Preferred Term– Safety Population (Japan)			Y
Table	14.3.1.2.1.3	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Population (Japan)			Y
Table	14.3.1.2.1.4	Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (<6 yrs, ≥6 yrs) by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.2.1.5	Treatment-Emergent Adverse Events with Decreased Appetite, Loss of appetite, or Hypophagia during Open-Label Treatment Periods – Safety Population (Japan)			Y
Table	14.3.1.3	TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.3.1	TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.4	Serious TEAEs by MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.4.1	Serious TEAEs by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.5.1	Related TEAEs MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.5.2	Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term -Safety population	Y	Y	
Table	14.3.1.5.3	Related TEAEs MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.5.4	Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term -Safety Population (Japan)			Y
Table	14.3.1.6	TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.6.1	TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.7	Overview of AESIs	Y	Y	
Table	14.3.1.7.1	Overview of AESIs - Safety Population (Japan)			Y
Table	14.3.1.8	Adverse events of special interest (AESI) by MedDRA System Organ Class and Preferred Term– Safety Population	Y	Y	
Table	14.3.1.8.1	Adverse events of special interest (AESI) by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.9.1	Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.1.1	Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.9.2	TEAEs starting in the 1st month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.2.1	TEAEs starting in the 1st month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.9.3	TEAEs starting in the 2nd month of OLE by MedDRA System Organ Class, , Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.3.1	TEAEs starting in the 2nd month of OLE by MedDRA System Organ Class, , Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.9.4	TEAEs starting in the 3rd month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.4.1	TEAEs starting in the 3rd month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.10.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days) – Safety Population			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.10.1.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days) – Safety Population (Japan)			Y
Table	14.3.1.10.2	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days) – Safety Population			
Table	14.3.1.10.2.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days) – Safety Population (Japan)			Y
	14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**			
Table	14.3.2.1	Listing of Deaths	Y	Y	
Table	14.3.2.1.1	Listing of Deaths (Japan)			Y
Table	14.3.2.2	Listing of SAEs	Y	Y	
Table	14.3.2.2.1	Listing of SAEs (Japan)			Y
Table	14.3.2.3	Listing of Discontinuations Due to AE	Y	Y	
Table	14.3.2.3.1	Listing of Discontinuations Due to AE (Japan)			Y
	14.3.4	**Laboratory value**			
Table	14.3.4.1	Laboratory parameters – Hematology– Safety Population	Y	Y	
Table	14.3.4.1.1	Laboratory parameters – Hematology– Safety Population (Japan)			Y
Table	14.3.4.2	Laboratory parameters – Biochemistry– Safety Population	Y	Y	
Table	14.3.4.2.1	Laboratory parameters – Biochemistry– Safety Population (Japan)			Y
Table	14.3.4.4.1	Laboratory parameters – Urinalysis (Quantitative variables) – Safety Population	Y	Y	
Table	14.3.4.4.1.1	Laboratory parameters – Urinalysis (Quantitative variables) – Safety Population (Japan)			Y
Table	14.3.4.4.2	Laboratory parameters – Urinalysis (Qualitative variables) – Safety Population	Y	Y	
Table	14.3.4.4.2.1	Laboratory parameters – Urinalysis (Qualitative variables) – Safety Population (Japan)			Y
Table	14.3.4.5	Laboratory parameters – Tests of growth, precocious puberty and thyroid function – Safety Population	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.4.5.1	Laboratory parameters – Tests of growth, precocious puberty and thyroid function – Safety Population (Japan)			Y
	14.4.1	**Vital Signs**			
Table	14.4.1.1	Vital signs parameters – Safety Population	Y	Y	
Table	14.4.1.1.1	Vital signs parameters – Safety Population (Japan)			Y
Figure	14.4.1.2	Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period – Safety Population		Y	
Figure	14.4.1.2.1	Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period – Safety Population (Japan)			
Table	14.4.1.3	Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics – Safety Population		Y	
Table	14.4.1.3.1	Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics – Safety Population (Japan)			Y
Table	14.4.1.4	Weight during the Open-Label Study Period over Time for De Novo Subjects: Summary Statistics – Safety Population			
Table	14.4.1.4.1	Weight during the Open-Label Study Period over Time for De Novo Subjects: Summary Statistics – Safety Population (Japan)			Y
Table	14.4.1.5	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period – Safety Population		Y	
Table	14.4.1.5.1	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period – Safety Population (Japan)			Y
Table	14.4.1.6	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate – Safety Population		Y	
Table	14.4.1.6.1	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate – Safety Population (Japan)			Y
Table	14.4.1.7	Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period – Safety Population		Y	
Table	14.4.1.7.1	Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period – Safety Population (Japan)			Y
Table	14.4.1.8	Weight Summary (Lost/Gain ≥5%) during Open-Label Study Period by Concomitant Topiramate – Safety Population		Y	
Table	14.4.1.8.1	Weight Summary (Lost/Gain ≥5%) during Open-Label Study Period by Concomitant Topiramate – Safety Population (Japan)			Y
	14.4.4	**Tanner Staging**			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.4.4.1	Tanner staging by age group for Boys– Safety Population	Y		
Table	14.4.4.1.1	Tanner staging by age group for Boys– Safety Population (Japan)			Y
Table	14.4.4.2	Tanner staging by age group for Girls– Safety Population	Y		
Table	14.4.4.2.1	Tanner staging by age group for Girls– Safety Population (Japan)			Y
	14.4.5	**Columbia-Suicide Severity Rating Scale (C-SSRS)**			
Table	14.4.5.1	Number of Subjects with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the C-SSRS during Treatment – Safety Population	Y	Y	
Table	14.4.5.1.1	Number of Subjects with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the C-SSRS during Treatment – Safety Population (Japan)			Y
Table	14.4.5.2	Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the C-SSRS during Treatment – Safety Population	Y		
Table	14.4.5.2.1	Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the C-SSRS during Treatment – Safety Population (Japan)			Y
	14.4.6	**Brief Rating Inventory of Executive Function-Preschool version (BRIEF)**			
Table	14.4.6.1	Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table – Safety population	Y	Y	
Table	14.4.6.1.1	Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table –Safety population (Japan)			Y
Table	14.4.6.2	Behavior Rating Inventory of Executive Function (BRIEF) – Scoring summary table – Safety population	Y	Y	
Table	14.4.6.2.1	Behavior Rating Inventory of Executive Function (BRIEF) – Scoring summary table – Safety population (Japan)			Y
Table	14.4.6.3	Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A) – Scoring summary table– Safety population (De Novo Subjects)			
Table	14.4.6.3.1	Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A)– Scoring summary table– Safety population (Japan) (De Novo Subjects)			Y
	16.2	**Subject data listing**			
	16.2.1	**Subject disposition and discontinuation**			
Listing	16.2.1.1	Subject completion/discontinuation	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.1.2	Subject completion/discontinuation (Japan)			Y
	16.2.2	**Protocol deviations**	Y		
Listing	16.2.2.1	Major Protocol Deviations	Y	Y	
Listing	16.2.2.2	Major Protocol Deviations (Japan)			Y
	16.2.3	**Subjects excluded from analysis**			
Listing	16.2.3.1	Subjects excluded from analysis populations	Y	Y	
Listing	16.2.3.1.1	Subjects excluded from analysis populations (Japan)			Y
Listing	16.2.3.2	Subject allocation to trial populations	Y	Y	
Listing	16.2.3.2.1	Subject allocation to trial populations (Japan)			Y
	16.2.4	**Demographic data and other baseline characteristics**			
Listing	16.2.4.1.1	Demographic data	Y	Y	
Listing	16.2.4.1.1.1	Demographic data (Japan)			Y
Listing	16.2.4.1.2	% Change from baseline in weight and BMI	Y	Y	
Listing	16.2.4.1.2.1	% Change from baseline in weight and BMI (Japan)			Y
Listing	16.2.4.2	Medical history			
Listing	16.2.4.3	Prior and concomitant medications and therapies/treatments	Y		
Listing	16.2.4.3.1	Prior and concomitant medications and therapies/treatments (Japan)			Y
Listing	16.2.4.4.1	Prior antiepileptic Drugs (AEDs)	Y	Y	
Listing	16.2.4.4.2	Concomitant antiepileptic Drugs (AEDs)	Y	Y	
Listing	16.2.4.4.3	Prior antiepileptic Drugs (AEDs) (Japan)			Y
Listing	16.2.4.4.4	Concomitant antiepileptic Drugs (AEDs) (Japan))			Y
Listing	16.2.4.5	Rescue medications	Y		
Listing	16.2.4.5.1	Rescue medications (Japan)			Y
	16.2.5	**Treatment exposure and compliance**			
Listing	16.2.5.1	IMP Intake per day during Treatment	Y	Y	
Listing	16.2.5.1.1	IMP Intake per day during Treatment (Japan)			Y
Listing	16.2.5.2	IMP Intake – self reported % compliance	Y	Y	
Listing	16.2.5.2.1	IMP Intake – self reported % compliance (Japan)			Y
Listing	16.2.5.3	Drug Accountability and Compliance to Study Treatment by Visit			
Listing	16.2.5.3.1	Drug Accountability and Compliance to Study Treatment by Visit (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
	16.2.6	**Effectiveness data**			
Listing	16.2.6.1	Convulsive seizure – duration and number of occurrences per subject (Diary data)	Y	Y	
Listing	16.2.6.1.1	Convulsive seizure – duration and number of occurrences per subject (Diary data) (Japan)			Y
Listing	16.2.6.2	Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data)	Y		
Listing	16.2.6.2.1	Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data) (Japan)			Y
Listing	16.2.6.3	Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject			
Listing	16.2.6.3.1	Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject (Japan)			Y
Listing	16.2.6.4	Percent reduction in convulsive seizure frequency from baseline	Y	Y	
Listing	16.2.6.4.1	Percent reduction in convulsive seizure frequency from baseline (Japan)			Y
Listing	16.2.6.5	Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator	Y	Y	
Listing	16.2.6.5.1	Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator (Japan)			Y
Listing	16.2.6.6	Quality of Life in Childhood Epilepsy Scale			
Listing	16.2.6.7	Quality of life of the Parent/Caregiver using EQ-5D-5L scale			
Listing	16.2.6.8	Quality of life of the Parent/Caregiver using HADS scale			
Listing	16.2.6.9.1	Pediatric Quality of Life Inventory (Peds QL) - for TODDLERS (age 2-4 years)			
Listing	16.2.6.9.2	Pediatric Quality of Life Inventory (Peds QL) - for Young Children (age 5-7 years)			
Listing	16.2.6.9.3	Pediatric Quality of Life Inventory (Peds QL) - for Children (age 8-12 years)			
Listing	16.2.6.9.4	Pediatric Quality of Life Inventory (Peds QL) - for TEENS (age 13-18 years)			
Listing	16.2.6.9.5	Pediatric Quality of Life Inventory (Peds QL) – Family Impact Module			
Listing	16.2.6.10	Study medication palatability assessment	Y		
Listing	16.2.6.11	Sleep quality and mealtime behavior			
Listing	16.2.6.12	Karolinska sleepiness scale			
Listing	16.2.6.13	Healthcare utilization questions			
	16.2.7	**Adverse events**			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.7.1	Adverse events	Y	Y	
Listing	16.2.7.2	Adverse events of special interests (AESI)	Y	Y	
	16.2.7.3	Adverse events for de novo subjects		Y (New)	
	16.2.8	**Laboratory data**			
Listing	16.2.8.1.1	Laboratory Data Hematology parameters	Y	Y	
Listing	16.2.8.1.1.1	Laboratory Data Hematology parameters (Japan)			Y
Listing	16.2.8.1.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Hematology	Y	Y	
Listing	16.2.8.1.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period – Hematology (Japan)			Y
Listing	16.2.8.2.1	Laboratory Data Biochemistry parameters	Y	Y	
Listing	16.2.8.2.1.1	Laboratory Data Biochemistry parameters (Japan)			Y
Listing	16.2.8.2.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Biochemistry	Y	Y	
Listing	16.2.8.2.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period – Biochemistry (Japan)			Y
Listing	16.2.8.3	Laboratory Data Coagulation parameters	Y	Y	
Listing	16.2.8.3.1	Laboratory Data Coagulation parameters (Japan)			Y
Listing	16.2.8.4.1	Laboratory Data Urinalysis parameters	Y	Y	
Listing	16.2.8.4.1.1	Laboratory Data Urinalysis parameters (Japan)			Y
Listing	16.2.8.4.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Urinalysis	Y	Y	
Listing	16.2.8.4.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Urinalysis (Japan)			Y
Listing	16.2.8.5	Tests of growth, precocious puberty and thyroid function	Y	Y	
Listing	16.2.8.5.1	Tests of growth, precocious puberty and thyroid function (Japan)			Y
Listing	16.2.8.6	Urine Pregnancy test	Y	Y	
Listing	16.2.8.6.1	Urine Pregnancy test (Japan)			Y
Listing	16.2.8.7	Urine THC panel	Y	Y	
Listing	16.2.8.7.1	Urine THC panel (Japan)			Y
Listing	16.2.8.8	Whole blood cannabidiol	Y	Y	
Listing	16.2.8.8.1	Whole blood cannabidiol (Japan)			Y
	16.2.9	**Other Safety Data**			
Listing	16.2.9.1.1	Vital signs	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.9.1.1.1	Vital signs (Japan)			Y
Listing	16.2.9.1.2	Abnormal Vital Signs Data	Y	Y	
Listing	16.2.9.1.2.1	Abnormal Vital Signs Data (Japan)			Y
Listing	16.2.9.1.9	Subjects with Weight Decrease >5% during Treatment	Y	Y	
Listing	16.2.9.1.9.1	Subjects with Weight Decrease >5% during Treatment (Japan)			Y
Listing	16.2.9.2	Columbia-Suicide Severity Rating Scale (C-SSRS)	Y	Y	
Listing	16.2.9.2.1	Columbia-Suicide Severity Rating Scale (C-SSRS) (Japan)			Y
Listing	16.2.9.3.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Individual Responses	Y	Y	
Listing	16.2.9.3.1.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Individual Responses (Japan)			Y
Listing	16.2.9.3.2	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Summary Scales	Y	Y	
Listing	16.2.9.3.2.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Summary Scales (Japan)			Y
Listing	16.2.9.3.3	Behavior Rating Inventory of Executive Function (BRIEF) – Individual Responses	Y	Y	
Listing	16.2.9.3.3.1	Behavior Rating Inventory of Executive Function (BRIEF) – Individual Responses (Japan)			Y
Listing	16.2.9.3.4	Behavior Rating Inventory of Executive Function (BRIEF) – Summary Scales	Y	Y	
Listing	16.2.9.3.4.1	Behavior Rating Inventory of Executive Function (BRIEF) – Summary Scales (Japan)			Y
Listing	16.2.9.3.5	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Individual Responses	Y	Y	
Listing	16.2.9.3.5.1	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Individual Responses (Japan)			Y
Listing	16.2.9.3.6	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Summary Scales	Y	Y	
Listing	16.2.9.3.6.1	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Summary Scales (Japan)			Y
Listing	16.2.9.4	Tanner Staging	Y	Y	
Listing	16.2.9.4.1	Tanner Staging (Japan)			Y
Listing	16.2.9.5	Physical Examination	Y	Y	
Listing	16.2.9.5.1	Physical Examination (Japan)			Y
Listing	16.2.9.6	Neurological Examination	Y	Y	
Listing	16.2.9.6.1	Neurological Examination (Japan)			Y

Shells of Tables, Data Listings, and Figures for Zogenix Study ZX008-1503

Programming notes are provided, as applicable, for each table and data listing.

The data listings will be sorted by treatment group in the Core Study and subjects will be identified and sorted by subject number.

The following programming notes apply to all tables (where applicable):

General Programming notes:

- In the Table header, Gp1, Gp2 etc should be replaced with the actual treatment group names
- Add missing categories where appropriate
- Percentages should be based on the number of non-missing subjects in the population in each treatment group (no percentage calculation should be performed and presented against the missing category)
- All listing displays for this open-label study are to be done by treatment group in the feeder study

Updated (01/15/2018)

- This Document provides TFLs for the study for the eventual final report. However, for interim reports, a subset of TFLs will be needed, and not all columns indicated in the TFL shells will be needed. For the NDA submission, programming will provide TFLs for only Group 9 (the "All subjects" column) in the TFLs.

Updated (14-Jul-2020)

- Adding in separate outputs for Japan. These will be replicate tables/listings of the existing outputs.

REVISION HISTORY

Date	Revision	Initials
13December2017	Based on SAP Version 0.3 for Protocol Amendment 3.0 dated 05may2017	GAS
01January	Clarified that only Group 9 (All Subjects) column will be used in the data presentations for the interim analysis	GAS
09January2018	Revised; included TFL shells for all efficacy and safety, and prioritization for interim analysis.	GAS
18Feb2018	Added age, gender and race to the AE listing mock	GAS
21Feb2018	Clarifying language added to QOLCE and PedsQL	GAS
11May2018	Updated Listings 16.2.9.3.1 – 16.2.9.3.4 - Headings for BRIEF-P and BRIEF	GAS
12Jul2018	Updated TFLs to include "n's" for the PROs	GAS
14JUL2020	Added Tables / listings for Japan	MLW
30JUL2020	Finalization for Japan Interim Analysis	MLW
04AUG2020	Signoff	MLW

Treatment Groups in Study ZX008-1503

Name of Treatment Group	Treatment Group Code	Description	AED Treatment from Feeder study	Feeder Study(s)	Approximate n
PBO-ZX008 OL	1	Placebo arms in all studies	Placebo in feeder study along with any protocol-approved background AED combination; no active ZX008	1501, 1502, 1504 Cohort 2	120
ZX 0.2 – ZX008 OL	2	0.2 arm in DB Studies	Any protocol-approved background AED combination; plus, ZX008 0.2 mg/kg/day max 30 mg	1501, 1502	80
ZX 0.8 – ZX008 OL	3	0.8 arm in DB studies	Any protocol-approved background AED combination; plus, ZX008 0.8 mg/kg/day max 30 mg	1501, 1502	80
ZX 0.5 – ZX008 OL	4	Active arm in 1504 cohort 2	Protocol-approved background regimen including STP + VPA + CBZ; plus ZX008 0.5 mg/kg/day max 20 mg	1504 Cohort 2	40
PK – ZX008 OL	5	Cohort 1 PK Study - Open label study		1504 Cohort 1	40
Summary Treatment Groups[1]					
ZX DBA – ZX008 OL	6 (Groups2-4)	All Active arms in the DB studies	Any protocol-approved background regimen, plus ZX008 at any protocol-approved dose – DB Studies only	1501, 1502, 1504 Cohort 2	200
ZX DB – ZX008 OL	7 (Groups1-4)	All subjects in randomized double-blind (DB) studies	Any protocol-approved background regimen at any protocol-approved dose – DB Studies only		
ZX – ZX008 OL	8 (Groups2-5)	All Active arms	Any protocol-approved background regimen, plus ZX008 at any protocol-approved dose – All studies	1501, 1502, 1504 Cohort 1, 1504 Cohort 2	240
ZX008 OL	9 (Groups1-5)	All Subjects in 1503 excluding de novo subjects	Any protocol-approved background regimen at any protocol-approved dose – All studies	1501, 1502, 1504 (both cohorts)	360
De Novo Subjects	10		Subjects entering 1503 who had not participated in any of the core studies	None	35

Notes:1: Subjects in 1504 cohort 1 do not have a pre-study treatment baseline for seizures and are not included in analyses requiring baseline (Core) seizure frequency.

Analysis Summary types

Type	Treatment By Groups (Codes as above)
A	1, 2, 3, 4,5,9, 10
B	1, 8, 9, 10
C	1, 6, 7, 10

NOTES:

The TFL shells provided are for the final study report. For the interim analysis, please note the following:

Programming Prioritization for Interim Analysis, 2018
Provide summaries for ZX008 OL (Group 9), i.e., "All Subjects" column only
1 = High priority -
2 = Medium Priority
3 = Low Priority

LIST OF TABLES, FIGURES AND LISTINGS FOR FINAL REPORT

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
	14.1	**Subject Information**			
	14.1.1	**Subject disposition, protocol deviations, and study populations**			
Table	14.1.1.1	Subject disposition – all enrolled subjects	Y	Y	
Table	14.1.1.1.1	Subject disposition – all enrolled subjects (Japan)			Y
Table	14.1.1.2	Major protocol deviations – Safety Population	Y	Y	
Table	14.1.1.2.1	Major protocol deviations – Safety Population (Japan)			Y
Table	14.1.1.3	Study Populations	Y		
Table	14.1.1.3.1	Study Populations (Japan)			Y
	14.1.2	**Demographic and baseline characteristics**			
Table	14.1.2.1	Demographic and baseline Characteristics – Safety Population	Y	Y	
Table	14.1.2.1.1	Demographic and baseline Characteristics – Safety Population (Japan)			Y
Table	14.1.2.2	Demographic and baseline Characteristics – mITT Population	Y		
Table	14.1.2.2.1	Demographic and baseline Characteristics – mITT Population (Japan)			Y
	14.1.3	**Medical history**			
Table	14.1.3.1	Medical history – Safety Population			
Table	14.1.3.1.1	Medical history – Safety Population (Japan)			Y
	14.1.4	**Prior/Baseline and concomitant medications and therapies/treatments**			
Table	14.1.4.1	Prior/Baseline medications and therapies/treatments – Safety Population			
Table	14.1.4.2	Concomitant medications and therapies/treatments – Safety Population			
Table	14.1.4.3	Prior/Baseline antiepileptic treatment – Safety Population		Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.1.4.3.1	Prior/Baseline antiepileptic treatment – Safety Population (Japan)			Y
Table	14.1.4.4.1	Concomitant antiepileptic treatment – Safety Population	Y	Y	
Table	14.1.4.4.1.1	Concomitant antiepileptic treatment – Safety Population (Japan)			Y
Table	14.1.4.4.2	Frequency Distribution for Number of Concomitant Antiepileptic Treatments-Safety Population	Y		
Table	14.1.4.4.2.1	Frequency Distribution for Number of Concomitant Antiepileptic Treatments-Safety Population (Japan)			Y
	14.1.5	**Treatment Exposure and compliance**			
Table	14.1.5.1	Duration of Treatment Exposure – Safety Population	Y	Y	
Table	14.1.5.1.1	Duration of Treatment Exposure by Age Group – Safety Population		Y	
Table	14.1.5.1.2	Duration of Treatment Exposure by Sex – Safety Population		Y	
Table	14.1.5.1.3	Duration of Treatment Exposure – Safety Population (Japan)			Y
Table	14.1.5.1.4	Duration of Treatment Exposure by Age Group – Safety Population (Japan)			Y
Table	14.1.5.1.5	Duration of Treatment Exposure by Sex – Safety Population (Japan)			Y
Table	14.1.5.1.6	Duration of Treatment Exposure in ZX008-1502 and ZX008-1503 Combined (Subjects Treated in ZX008-1502 or ZX008-1503) (Japan)			Y
Table	14.1.5.1.7.1	Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit – Safety Population			
Table	14.1.5.1.7.2	Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit – Safety Population (Japan)			Y
Table	14.1.5.1.8.1	Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment – Safety Population			
Table	14.1.5.1.8.2	Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment – Safety Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.1.5.1.9.1	Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment – Safety Population			
Table	14.1.5.1.9.2	Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment – Safety Population (Japan)			Y
Table	14.1.5.1.10.1	Number of Subjects Receiving ZX008 According to Actual Dose (mg/kg) and Duration of Treatment – Safety Population			
Table	14.1.5.1.10.2	Number of Subjects Receiving ZX008 According to Actual Dose (mg/kg) and Duration of Treatment – Safety Population (Japan)			Y
Table	14.1.5.2.1	Compliance to IMP intake – Safety Population	Y	Y	
Table	14.1.5.2.1.1	Compliance to IMP intake – Safety Population (Japan)			Y
Table	14.1.5.2.2	Compliance to IMP intake – mITT Population	Y	Y	
Table	14.1.5.2.2.1	Compliance to IMP intake – mITT Population (Japan)			Y
	14.2	**Effectiveness**			
	14.2.1	**Effectiveness – Convulsive Seizure Frequency**			
Table	14.2.1.1.1	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics and Tests of Changes from Baseline	Y	Y	
Table	14.2.1.1.2	Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group: Summary statistics and Tests of Changes from Baseline – mITT Population	Y		
Table	14.2.1.1.3	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary Statistics and Tests of Changes from Baseline –mITT Population	Y		
Table	14.2.1.1.4	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, , by Age Group: Summary Statistics and Tests of Changes from Baseline – mITT Population	Y		
Table	14.2.1.1.5	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics – 1504 Cohort 1 Subjects	Y		

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.2.1.1.6	Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.1.7	Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group: Summary Statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.1.8	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary statistics and Tests of Changes from Baseline –mITT Population (Japan)			Y
Table	14.2.1.1.9	Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, by Age Group: Summary statistics and Tests of Changes from Baseline – mITT Population (Japan)			Y
Table	14.2.1.2	Convulsive seizure frequency per 28 days - Endpoint: Parametric analysis – mITT Population			
Table	14.2.1.3	Convulsive seizure frequency per 28 days - Endpoint: Nonparametric analysis – mITT Population			
Table	14.2.1.4	Convulsive seizure frequency per 28 days, Over Time - Parametric analysis – mITT Population			
Table	14.2.1.5	Convulsive seizure frequency per 28 days, Over Time, Using Mean Daily Dose: Parametric Analysis – mITT Population			
Table	14.2.1.6	% of subjects with Changes in AED medications during the first 6 months of the OLE Treatment Period – mITT Population			
Figure	14.2.1.7	Graph of means for convulsive seizure frequency per 28 days - mITT Population			
Figure	14.2.1.8	Graph of model adjusted means for Convulsive seizure frequency per 28 days – mITT Population			
Figure	14.2.1.9	Graph of convulsive frequency per 28 days, Over Time, Using Mean Daily Dose – mITT Population			
	14.2.2	**Effectiveness – Proportion of responders for convulsive seizure frequency**			
Table	14.2.2.1	Percent reduction in convulsive seizure frequency, OLE Treatment Period– mITT population	Y	Y	
Table	14.2.2.1.1	Percent reduction in convulsive seizure frequency, OLE Treatment Period– mITT population (Japan)			Y
Figure	14.2.2.2	Cumulative response curves for percent reduction in CSF during OLE Treatment Period – mITT population	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Figure	14.2.2.2.1	Cumulative response curves for percent reduction in CSF during OLE Treatment Period – mITT population			Y
	14.2.3	**Effectiveness – Duration of Longest interval between convulsive seizures**			
Table	14.2.3.1	Duration of Longest interval between convulsive seizures during OLE Treatment Period – mITT Population			
Figure	14.2.3.2	Boxplot of distribution of duration of longest interval between convulsive seizures during OLE Treatment Period – mITT Population			
	14.2.4	**Effectiveness – Summary of duration of convulsive episodes**			
Table	14.2.4.1	Summary of Duration of Convulsive Seizure Episodes during OLE Treatment Period - mITT Population			
Table	14.2.4.2	Summary of Gaps between Convulsive Seizure Episodes during OLE Treatment Period mITT Population			
	14.2.5	**Effectiveness – Number of convulsive seizure free days**			
Table	14.2.5.1	Convulsive seizure-free days – summary statistics – mITT Population			
Table	14.2.5.2	Convulsive seizure-free days – Parametric Analysis by Age Group - mITT Population			
Table	14.2.5.3	Convulsive seizure-free days – Parametric Analysis by Mean Daily Dose - mITT Population			
Table	14.2.5.4	Convulsive seizure-free days – summary statistics for subjects from Study 1504 –Cohort 1			
	14.2.6	**Effectiveness –non-convulsive and convulsive seizure frequency**			
Table	14.2.6.1	Non-convulsive seizure frequency during OLE Treatment Period – mITT Population			
Table	14.2.6.2	Convulsive + non-convulsive seizure frequency during OLE Treatment Period – mITT Population			
	14.2.7	**Effectiveness – Incidence of rescue medication**			
Table	14.2.7.1	Days with Rescue medication usage during OLE Treatment Period – mITT Population	Y		
Table	14.2.7.2	Days with Rescue medication usage during OLE Treatment Period – mITT Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
	14.2.8	**Effectiveness – Incidence of hospitalization to treat seizure**			
Table	14.2.8.1	Hospitalization and Other Healthcare Resource Utilization to Treat Seizure - mITT Population– mITT Population			
Table	14.2.8.2	Hospitalization and Other Healthcare Resource Utilization to Treat Seizure - mITT Population– mITT Population (Japan)			**Y**
	14.2.9	**Effectiveness – Incidence of status epilepticus**			
Table	14.2.9.1	Number of episodes of status epilepticus during OLE Treatment Period - mITT Population			
Table	14.2.9.1.1	Number of episodes of status epilepticus during OLE Treatment Period - mITT Population (Japan)			Y
Table	14.2.9.2	Duration of Seizures – mITT Population			
	14.2.10	**Effectiveness – Clinical Global Impression** of Improvement, **– Rating by Parent/Caregiver and Investigator**			
Table	14.2.10.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population	Y		
Table	14.2.10.1.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population (Japan)			Y
Figure	14.2.10.2	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population	Y		
Figure	14.2.10.2.1	Clinical Global Impression of Improvement, Parent/Caregiver Rating – mITT Population (Japan)			Y
Table	14.2.10.3	Clinical Global Impression of Improvement, Investigator Rating – mITT Population	Y		
Table	14.2.10.3.1	Clinical Global Impression of Improvement, Investigator Rating – mITT Population (Japan)			Y
Figure	14.2.10.4	Clinical Global Impression of Improvement,, Investigator Rating – mITT Population	Y		
Figure	14.2.10.4.1	Clinical Global Impression of Improvement,, Investigator Rating – mITT Population (Japan)			Y
	14.2.11	**Effectiveness – Quality of Life in Childhood Epilepsy Scale**			
Table	14.2.11.1	Quality of Life in Childhood Epilepsy (QOLCE) – mITT population			
	14.2.12	**Effectiveness – Peds QL**			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.2.12.1	PedsQL Pediatric Quality of Life Inventory (Version 4.0) - Parent Report – mITT Population			
Table	14.2.12.2	PedsQL Family Impact Module (Version 2.0) – Parent Report – mITT Population			
	14.2.13	**Effectiveness –Quality of Life of the Parent /Caregiver using EQ-5D-5L Sale**			
Table	14.2.13.1	QOL of Parent/Caregiver using EQ-5D-5L –QOL of Parent/Caregiver Based on EQ-5D-5L: Health Profile Summary Original Response Categories – mITT Population			
Table	14.2.13.2	QOL of Parent/Caregiver Based on EQ-5D-5L: Health Profile Summary Using Dichotomized Response Categories – mITT Population			
Table	14.2.13.3	QOL of Parent/Caregiver Based on EQ-5D-5L: Overall Health Status Using VAS (0-100) Scale - mITT Population			
	14.2.14	**Effectiveness –Quality of Life of the Parent /Caregiver using HADS Scale**			
Table	14.2.14.1	Parent/Caregiver Ratings Based on Hospital Anxiety and Depression Scale (HADS): Normal; Borderline Abnormal; and Abnormal Categories – mITT population			
Table	14.2.14.2	Parent/Caregiver ratings Based on Hospital Anxiety and Depression Scale (HADS): Total Score – mITT population			
	14.2.15	**Exploratory objectives (feeder study ZX008-1504 subjects only)**			
Table	14.2.15.1	Study medication palatability assessment	Y		
Table	14.2.15.2	Sleep quality and mealtime behavior – mITT population			
Table	14.2.15.3	Karolinska sleepiness scale – mITT population			
	14.3	**Safety**			
	14.3.1	**Summary of adverse events**			
Table	14.3.1.1	Overview of number of subjects with TEAE during OLE Treatment Period – Safety Population	Y	Y	
Table	14.3.1.1.1	Overview of number of subjects with TEAE during OLE Treatment Period – Safety Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.2.1	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Population	Y	Y	
Table	14.3.1.2.1.1	Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (< 6 yrs, ≥6 yrs) by MedDRA System Organ Class and Preferred Term – Safety Population		Y	
Table	14.3.1.2.1.2	Treatment-Emergent Adverse Events with Decreased Appetite, Loss of appetite, or Hypophagia during Open-Label Treatment Periods – Safety Population		Y	
Table	14.3.1.2.2	Treatment-Emergent Adverse Events occurring in ≥5% of subjects by MedDRA System Organ Class and Preferred Term– Safety population	Y	Y	
Table	14.3.1.2.2.1	Treatment-Emergent Adverse Events occurring in ≥5% of subjects by MedDRA System Organ Class and Preferred Term– Safety Population (Japan)			Y
Table	14.3.1.2.1.3	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Population (Japan)			Y
Table	14.3.1.2.1.4	Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (<6 yrs, ≥6 yrs) by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.2.1.5	Treatment-Emergent Adverse Events with Decreased Appetite, Loss of appetite, or Hypophagia during Open-Label Treatment Periods – Safety Population (Japan)			Y
Table	14.3.1.3	TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.3.1	TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.4	Serious TEAEs by MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.4.1	Serious TEAEs by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.5.1	Related TEAEs MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.5.2	Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term -Safety population	Y	Y	
Table	14.3.1.5.3	Related TEAEs MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.5.4	Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term -Safety Population (Japan)			Y
Table	14.3.1.6	TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term – Safety Population	Y	Y	
Table	14.3.1.6.1	TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.7	Overview of AESIs	Y	Y	
Table	14.3.1.7.1	Overview of AESIs - Safety Population (Japan)			Y
Table	14.3.1.8	Adverse events of special interest (AESI) by MedDRA System Organ Class and Preferred Term– Safety Population	Y	Y	
Table	14.3.1.8.1	Adverse events of special interest (AESI) by MedDRA System Organ Class and Preferred Term – Safety Population (Japan)			Y
Table	14.3.1.9.1	Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.1.1	Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.9.2	TEAEs starting in the 1st month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.2.1	TEAEs starting in the 1st month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.1.9.3	TEAEs starting in the 2nd month of OLE by MedDRA System Organ Class, , Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.3.1	TEAEs starting in the 2nd month of OLE by MedDRA System Organ Class, , Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.9.4	TEAEs starting in the 3rd month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population	Y		
Table	14.3.1.9.4.1	TEAEs starting in the 3rd month of OLE by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study – Safety Population (Japan)			Y
Table	14.3.1.10.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days) – Safety Population			
Table	14.3.1.10.1.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days) – Safety Population (Japan)			Y
Table	14.3.1.10.2	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days) – Safety Population			
Table	14.3.1.10.2.1	Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days) – Safety Population (Japan)			Y
	14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**			
Table	14.3.2.1	Listing of Deaths	Y	Y	
Table	14.3.2.1.1	Listing of Deaths (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.3.2.2	Listing of SAEs	Y	Y	
Table	14.3.2.2.1	Listing of SAEs (Japan)			Y
Table	14.3.2.3	Listing of Discontinuations Due to AE	Y	Y	
Table	14.3.2.3.1	Listing of Discontinuations Due to AE (Japan)			Y
	14.3.4	**Laboratory value**			
Table	14.3.4.1	Laboratory parameters – Hematology– Safety Population	Y	Y	
Table	14.3.4.1.1	Laboratory parameters – Hematology– Safety Population (Japan)			Y
Table	14.3.4.2	Laboratory parameters – Biochemistry– Safety Population	Y	Y	
Table	14.3.4.2.1	Laboratory parameters – Biochemistry– Safety Population (Japan)			Y
Table	14.3.4.4.1	Laboratory parameters – Urinalysis (Quantitative variables) – Safety Population	Y	Y	
Table	14.3.4.4.1.1	Laboratory parameters – Urinalysis (Quantitative variables) – Safety Population (Japan)			Y
Table	14.3.4.4.2	Laboratory parameters – Urinalysis (Qualitative variables) – Safety Population	Y	Y	
Table	14.3.4.4.2.1	Laboratory parameters – Urinalysis (Qualitative variables) – Safety Population (Japan)			Y
Table	14.3.4.5	Laboratory parameters – Tests of growth, precocious puberty and thyroid function – Safety Population	Y	Y	
Table	14.3.4.5.1	Laboratory parameters – Tests of growth, precocious puberty and thyroid function – Safety Population (Japan)			Y
	14.4.1	**Vital Signs**			
Table	14.4.1.1	Vital signs parameters – Safety Population	Y	Y	
Table	14.4.1.1.1	Vital signs parameters – Safety Population (Japan)			Y
Figure	14.4.1.2	Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period – Safety Population		Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Figure	14.4.1.2.1	Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period – Safety Population (Japan)			
Table	14.4.1.3	Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics – Safety Population		Y	
Table	14.4.1.3.1	Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics – Safety Population (Japan)			Y
Table	14.4.1.4	Weight during the Open-Label Study Period over Time for De Novo Subjects: Summary Statistics – Safety Population			
Table	14.4.1.4.1	Weight during the Open-Label Study Period over Time for De Novo Subjects: Summary Statistics – Safety Population (Japan)			Y
Table	14.4.1.5	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period – Safety Population		Y	
Table	14.4.1.5.1	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period – Safety Population (Japan)			Y
Table	14.4.1.6	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate – Safety Population		Y	
Table	14.4.1.6.1	Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate – Safety Population (Japan)			Y
Table	14.4.1.7	Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period – Safety Population		Y	
Table	14.4.1.7.1	Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period – Safety Population (Japan)			Y
Table	14.4.1.8	Weight Summary (Lost/Gain ≥5%) during Open-Label Study Period by Concomitant Topiramate – Safety Population		Y	
Table	14.4.1.8.1	Weight Summary (Lost/Gain ≥5%) during Open-Label Study Period by Concomitant Topiramate – Safety Population (Japan)			Y
	14.4.4	**Tanner Staging**			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.4.4.1	Tanner staging by age group for Boys– Safety Population	Y		
Table	14.4.4.1.1	Tanner staging by age group for Boys– Safety Population (Japan)			Y
Table	14.4.4.2	Tanner staging by age group for Girls– Safety Population	Y		
Table	14.4.4.2.1	Tanner staging by age group for Girls– Safety Population (Japan)			Y
	14.4.5	**Columbia-Suicide Severity Rating Scale (C-SSRS)**			
Table	14.4.5.1	Number of Subjects with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the C-SSRS during Treatment – Safety Population	Y	Y	
Table	14.4.5.1.1	Number of Subjects with Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior without Suicidal Intent Based on the C-SSRS during Treatment – Safety Population (Japan)			Y
Table	14.4.5.2	Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the C-SSRS during Treatment – Safety Population	Y		
Table	14.4.5.2.1	Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the C-SSRS during Treatment – Safety Population (Japan)			Y
	14.4.6	**Brief Rating Inventory of Executive Function-Preschool version (BRIEF)**			
Table	14.4.6.1	Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table – Safety population	Y	Y	
Table	14.4.6.1.1	Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table –Safety population (Japan)			Y
Table	14.4.6.2	Behavior Rating Inventory of Executive Function (BRIEF) – Scoring summary table – Safety population	Y	Y	
Table	14.4.6.2.1	Behavior Rating Inventory of Executive Function (BRIEF) – Scoring summary table – Safety population (Japan)			Y
Table	14.4.6.3	Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A) – Scoring summary table– Safety population (De Novo Subjects)			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Table	14.4.6.3.1	Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A)– Scoring summary table– Safety population (Japan) (De Novo Subjects)			Y
	16.2	**Subject data listing**			
	16.2.1	**Subject disposition and discontinuation**			
Listing	16.2.1.1	Subject completion/discontinuation	Y	Y	
Listing	16.2.1.2	Subject completion/discontinuation (Japan)			Y
	16.2.2	**Protocol deviations**	Y		
Listing	16.2.2.1	Major Protocol Deviations	Y	Y	
Listing	16.2.2.2	Major Protocol Deviations (Japan)			Y
	16.2.3	**Subjects excluded from analysis**			
Listing	16.2.3.1	Subjects excluded from analysis populations	Y	Y	
Listing	16.2.3.1.1	Subjects excluded from analysis populations (Japan)			Y
Listing	16.2.3.2	Subject allocation to trial populations	Y	Y	
Listing	16.2.3.2.1	Subject allocation to trial populations (Japan)			Y
	16.2.4	**Demographic data and other baseline characteristics**			
Listing	16.2.4.1.1	Demographic data	Y	Y	
Listing	16.2.4.1.1.1	Demographic data (Japan)			Y
Listing	16.2.4.1.2	% Change from baseline in weight and BMI	Y	Y	
Listing	16.2.4.1.2.1	% Change from baseline in weight and BMI (Japan)			Y
Listing	16.2.4.2	Medical history			
Listing	16.2.4.3	Prior and concomitant medications and therapies/treatments	Y		

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.4.3.1	Prior and concomitant medications and therapies/treatments (Japan)			Y
Listing	16.2.4.4.1	Prior antiepileptic Drugs (AEDs)	Y	Y	
Listing	16.2.4.4.2	Concomitant antiepileptic Drugs (AEDs)	Y	Y	
Listing	16.2.4.4.3	Prior antiepileptic Drugs (AEDs) (Japan)			Y
Listing	16.2.4.4.4	Concomitant antiepileptic Drugs (AEDs) (Japan))			Y
Listing	16.2.4.5	Rescue medications	Y		
Listing	16.2.4.5.1	Rescue medications (Japan)			Y
	16.2.5	**Treatment exposure and compliance**			
Listing	16.2.5.1	IMP Intake per day during Treatment	Y	Y	
Listing	16.2.5.1.1	IMP Intake per day during Treatment (Japan)			Y
Listing	16.2.5.2	IMP Intake – self reported % compliance	Y	Y	
Listing	16.2.5.2.1	IMP Intake – self reported % compliance (Japan)			Y
Listing	16.2.5.3	Drug Accountability and Compliance to Study Treatment by Visit			
Listing	16.2.5.3.1	Drug Accountability and Compliance to Study Treatment by Visit (Japan)			Y
	16.2.6	**Effectiveness data**			
Listing	16.2.6.1	Convulsive seizure – duration and number of occurrences per subject (Diary data)	Y	Y	
Listing	16.2.6.1.1	Convulsive seizure – duration and number of occurrences per subject (Diary data) (Japan)			Y
Listing	16.2.6.2	Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data)	Y		
Listing	16.2.6.2.1	Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data) (Japan)			Y
Listing	16.2.6.3	Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject			

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.6.3.1	Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject (Japan)			Y
Listing	16.2.6.4	Percent reduction in convulsive seizure frequency from baseline	Y	Y	
Listing	16.2.6.4.1	Percent reduction in convulsive seizure frequency from baseline (Japan)			Y
Listing	16.2.6.5	Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator	Y	Y	
Listing	16.2.6.5.1	Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator (Japan)			Y
Listing	16.2.6.6	Quality of Life in Childhood Epilepsy Scale			
Listing	16.2.6.7	Quality of life of the Parent/Caregiver using EQ-5D-5L scale			
Listing	16.2.6.8	Quality of life of the Parent/Caregiver using HADS scale			
Listing	16.2.6.9.1	Pediatric Quality of Life Inventory (Peds QL) - for TODDLERS (age 2-4 years)			
Listing	16.2.6.9.2	Pediatric Quality of Life Inventory (Peds QL) - for Young Children (age 5-7 years)			
Listing	16.2.6.9.3	Pediatric Quality of Life Inventory (Peds QL) - for Children (age 8-12 years)			
Listing	16.2.6.9.4	Pediatric Quality of Life Inventory (Peds QL) - for TEENS (age 13-18 years)			
Listing	16.2.6.9.5	Pediatric Quality of Life Inventory (Peds QL) – Family Impact Module			
Listing	16.2.6.10	Study medication palatability assessment	Y		
Listing	16.2.6.11	Sleep quality and mealtime behavior			
Listing	16.2.6.12	Karolinska sleepiness scale			
Listing	16.2.6.13	Healthcare utilization questions			
	16.2.7	**Adverse events**			
Listing	16.2.7.1	Adverse events	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.7.2	Adverse events of special interests (AESI)	Y	Y	
	16.2.7.3	Adverse events for de novo subjects		Y (New)	
	16.2.8	**Laboratory data**			
Listing	16.2.8.1.1	Laboratory Data Hematology parameters	Y	Y	
Listing	16.2.8.1.1.1	Laboratory Data Hematology parameters (Japan)			Y
Listing	16.2.8.1.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Hematology	Y	Y	
Listing	16.2.8.1.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period – Hematology (Japan)			Y
Listing	16.2.8.2.1	Laboratory Data Biochemistry parameters	Y	Y	
Listing	16.2.8.2.1.1	Laboratory Data Biochemistry parameters (Japan)			Y
Listing	16.2.8.2.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Biochemistry	Y	Y	
Listing	16.2.8.2.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period – Biochemistry (Japan)			Y
Listing	16.2.8.3	Laboratory Data Coagulation parameters	Y	Y	
Listing	16.2.8.3.1	Laboratory Data Coagulation parameters (Japan)			Y
Listing	16.2.8.4.1	Laboratory Data Urinalysis parameters	Y	Y	
Listing	16.2.8.4.1.1	Laboratory Data Urinalysis parameters (Japan)			Y
Listing	16.2.8.4.2	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Urinalysis	Y	Y	
Listing	16.2.8.4.2.1	Most Abnormal Laboratory Parameters during Open-label Treatment Period - Urinalysis (Japan)			Y
Listing	16.2.8.5	Tests of growth, precocious puberty and thyroid function	Y	Y	
Listing	16.2.8.5.1	Tests of growth, precocious puberty and thyroid function (Japan)			Y
Listing	16.2.8.6	Urine Pregnancy test	Y	Y	
Listing	16.2.8.6.1	Urine Pregnancy test (Japan)			Y

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.8.7	Urine THC panel	Y	Y	
Listing	16.2.8.7.1	Urine THC panel (Japan)			Y
Listing	16.2.8.8	Whole blood cannabidiol	Y	Y	
Listing	16.2.8.8.1	Whole blood cannabidiol (Japan)			Y
	16.2.9	**Other Safety Data**			
Listing	16.2.9.1.1	Vital signs	Y	Y	
Listing	16.2.9.1.1.1	Vital signs (Japan)			Y
Listing	16.2.9.1.2	Abnormal Vital Signs Data	Y	Y	
Listing	16.2.9.1.2.1	Abnormal Vital Signs Data (Japan)			Y
Listing	16.2.9.1.9	Subjects with Weight Decrease >5% during Treatment	Y	Y	
Listing	16.2.9.1.9.1	Subjects with Weight Decrease >5% during Treatment (Japan)			Y
Listing	16.2.9.2	Columbia-Suicide Severity Rating Scale (C-SSRS)	Y	Y	
Listing	16.2.9.2.1	Columbia-Suicide Severity Rating Scale (C-SSRS) (Japan)			Y
Listing	16.2.9.3.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Individual Responses	Y	Y	
Listing	16.2.9.3.1.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Individual Responses (Japan)			Y
Listing	16.2.9.3.2	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Summary Scales	Y	Y	
Listing	16.2.9.3.2.1	Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) – Summary Scales (Japan)			Y
Listing	16.2.9.3.3	Behavior Rating Inventory of Executive Function (BRIEF) – Individual Responses	Y	Y	
Listing	16.2.9.3.3.1	Behavior Rating Inventory of Executive Function (BRIEF) – Individual Responses (Japan)			Y
Listing	16.2.9.3.4	Behavior Rating Inventory of Executive Function (BRIEF) – Summary Scales	Y	Y	

Table/ Figure/ Listing	Number	Table Header	Included in Interim Analysis?	Include in 120-day safety update report	Included in 1503 Japan safety update report, 2020
Listing	16.2.9.3.4.1	Behavior Rating Inventory of Executive Function (BRIEF) – Summary Scales (Japan)			Y
Listing	16.2.9.3.5	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Individual Responses	Y	Y	
Listing	16.2.9.3.5.1	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Individual Responses (Japan)			Y
Listing	16.2.9.3.6	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Summary Scales	Y	Y	
Listing	16.2.9.3.6.1	Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) – Summary Scales (Japan)			Y
Listing	16.2.9.4	Tanner Staging	Y	Y	
Listing	16.2.9.4.1	Tanner Staging (Japan)			Y
Listing	16.2.9.5	Physical Examination	Y	Y	
Listing	16.2.9.5.1	Physical Examination (Japan)			Y
Listing	16.2.9.6	Neurological Examination	Y	Y	
Listing	16.2.9.6.1	Neurological Examination (Japan)			Y

Table 14.1.1.1
Subject Disposition
All Enrolled Subjects

Part 1 of 2

	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=xx)	De Novo Subjects (N=xx)
Enrolled	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Subjects discontinued trial	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Reasons for trial discontinuation							
Reason 1	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Reason 2	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
---	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
---	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Completed Study*	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)

Note: Percentages for summaries where only a Total column is present use number of enrolled subjects as the denominator.
*Study is an ongoing open-label extension. Amendment 4 allows de novo subjects to be enrolled.

Programming Notes:

- Information on this table comes from CRF pages 6, 14, 33 and 34.
- For 120 day safety update – One column only for this table– ZX008 OL
- For 15Feb2019 IDSMC, please add the following note:

"Note: A total of 10 de novo subjects enrolled as of the data cutoff date for this report (15FEB2019) are not included in the tables but are included in the listings. None of those subjects has withdrawn from the study as of the data cutoff date." Add only for the IDSMC output.

For 120-day output: *Study is an ongoing open-label extension. Amendment 4 allows de novo subjects to be enrolled. A total of 10 de novo subjects enrolled as of the data cutoff date for this report (15FEB2019) are not included in the tables, figures and listings."

Table 14.1.1.1
Subject Disposition
All Enrolled Subjects

Part 2 of 2

	Gp1 (N = XX) [1]	Gp8 (N = XX) [2]	Gp9 (N = XX)
Enrolled	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Subjects discontinued trial early:	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Reasons for early trial discontinuation:			
Reason 1	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Reason 2	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
---	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
---	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Completed study	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)

Programming Notes:

- Information on this table comes from CRF 6, 14, 33 and 34.

Treatment Group for Part 2 of 2:
Groups 1, 6 and 7

Programming Notes: Use the shell for 14.1.1.1 for

Table 14.1.1.1.1
Subject disposition
All Enrolled Subject (Japan).

Table 14.1.1.2
Major protocol deviations
Safety Population

	Gp1 (N = XX) [1]	Gp8 (N = XX) [2]	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
No. (%) Subjects with at Least One MPD	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
Type of MPD				
MPD 1	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
MPD 2	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
MPD 3	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)

MPD = Major protocol deviation
Note: Subjects may have had more than one MPD.

Programming Note: Use the shell for 14.1.1.2 for

Table 14.1.1.2.1
Major protocol deviations
Safety Population (Japan)

Table 14.1.1.3
Study Populations

	Gp1 (N=xx)	Gp2 (N=xx)	Gp3 (N=xx)	Gp4 (N=xx)	Gp5 (N=xx)	Gp9 (N=XXX)	De Novo Subjects (N=xxx)
Enrolled (ITT) Population[1]	XX	XX	XX	XX	XX	XX	XX
Modified ITT (mITT) Population[2]	XX	XX	XX	XX	XX	XX	XX
Safety (SAF) Population [3]	XX	XX	XX	XX	XX	XX	XX

Notes:
[1] Enrolled (ITT) population: All subjects who gave informed consent or assent for entry into Study ZX008-1503.
[2] Modified ITT Population: All enrolled subjects who receive at least one dose of ZX008 and for whom at least 30 days of diary data are available. [All subjects on study from Day 30 of OLE period onward are included in the mITT population.]
[3] Safety population: All subjects who received at least one dose of ZX008 during the open label extension.

Programming note: For [2] include any subject who has any data from Study Day 30 onward.

Programming note: Use the shell for 14.1.1.3 for

Table 14.1.1.3.1
Study Populations (Japan)

Table 14.1.2.1
Demographic and Baseline Characteristics
Safety Population

	Gp1 (N=xx)	Gp2 (N=xx)	Gp3 (N=xx)	Gp4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=XXX)	De Novo Subjects (N=xxx)
Age (years)							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX	XX
Age Group, n (%)							
<6 Years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6-18 Years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>18 Years							
Sex							
Male	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Female	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Race[ADSL.RACE]							
White	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Black or African American	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Asian	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
American Indian or Alaska native	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Native Hawaiian or Other Pacific Islander	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other[ADSL.RACEOTH]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

	Gp1 (N=xx)	Gp2 (N=xx)	Gp3 (N=xx)	Gp4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=XXX)	De Novo Subjects (N=xxx)
Not Reported	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ethnic Group							
Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Hispanic or Latino	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not Reported[*]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unknown[*]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Baseline Height (m)							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
SD	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Min	XXX	XXX	XXX	XXX	XXX	XXX	XXX
Max	XXX	XXX	XXX	XXX	XXX	XXX	XXX
Baseline Weight (kg)							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
SD	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Min	XXX	XXX	XXX	XXX	XXX	XXX	XXX
Max	XXX	XXX	XXX	XXX	XXX	XXX	XXX
Baseline BMI (kg/m^2)							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX

	Gp1 (N=xx)	Gp2 (N=xx)	Gp3 (N=xx)	Gp4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=XXX)	De Novo Subjects (N=xxx)
Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Min	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Max	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

*Not reported, or missing: Privacy laws in some regions/countries preclude disclosure of certain personal information.
BMI=Body Mass Index, where BMI = weight (kg) / height (m^2).
Note: Percentages are calculated based on the number of subjects with non-missing data in the Safety population.
Subjects do not necessarily reside in the country in which they attend clinic for the purpose of this study.

Programming note: Use the shell for Table 14.1.2.1 for

Table 14.1.2.1.1
Demographic and Baseline Characteristics
Safety Population (Japan)

Table 14.1.2.2
Demographic and Baseline Characteristics
mITT Population

Table 14.1.2.2.1
Demographic and Baseline Characteristics
mITT Population (Japan)

Table 14.1.3.1
Medical History
Safety Population

MedDRA [1] System Organ Class and Preferred Term	Gp1 (N = XX)	Gp8 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One Previous or Concurrent Medical History	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…				
…				

[1] MedDRA : Medical Dictionary for Regulatory Activities – latest version at the time of data collection.

Programming note: Use the shell for 14.1.3.1 for

Table 14.1.3.1.1
Medical History
Safety Population (Japan)

Table 14.1.4.1
Prior Medications and Therapies/Treatments
Safety Population

Drug Class ATC Level 2 [1] Preferred Term	Gp1 (N = XX)	Gp8 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One prior Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
DRUG CLASS	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…				
…				

[1] Medication terms are coded using the World Health Organization (WHO) Drug Dictionary – latest version.

Table 14.1.4.2
Concomitant Medications and Therapies/Treatments
Safety Population

Drug Class ATC Level 2 Preferred Term [1]	Gp1 (N = XX)	Gp8 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One Concomitant Medication	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
DRUG CLASS	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…				
…				

[1] Medication terms are coded using the World Health Organization (WHO) Drug Dictionary – latest version.

Table 14.1.4.3
Prior/Baseline Antiepileptic Treatment
Safety Population

Drug Class ATC Level 2 Preferred Term [1]	Gp1 (N = XX)	Gp8 (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One prior Antiepileptic treatment	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
DRUG CLASS	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…				
…				

[1] Medication terms are coded using the World Health Organization (WHO) Drug Dictionary – latest version.
Note: Multiple occurrences of the same Antiepileptic treatment are counted once for each subject within a drug class and preferred drug name.

Programming Note: Use the shell for 14.1.4.3 for

Table 14.1.4.3.1
Prior/Baseline Antiepileptic Treatment
Safety Population (Japan)

Table 14.1.4.4.1
Concomitant Antiepileptic Treatment
Safety Population

Drug Class ATC Level 2 Preferred Term [1]	Gp1 (N = XX)	Gp8 (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One Concomitant antiepileptic treatment	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
DRUG CLASS	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Name 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
…				
…				

[1] Medication terms are coded using the World Health Organization (WHO) Drug Dictionary – latest version.
Note: Multiple occurrences of the same antiepileptic treatment are counted once for each subject within a drug class and preferred drug name.
Note: A concomitant antiepileptic treatment (AEDs) defined as antiepileptic treatment with a start or stop date after the first dose of study treatment. Missing or partial start or stop dates for concomitant AEDs are handled as specified in SAP Section 6.2.5

Programming Note: Use the shell for 14.1.4.4.1 for

Table 14.1.4.4.1.1
Concomitant Antiepileptic Treatment
Safety Population (Japan)

Table 14.1.4.4.2
Frequency Distribution for Number of Concomitant Antiepileptic Drugs
Safety Population

	Gp1 (N = XX)	Gp8 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N = XX)
Number of Concomitant AED				
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

AED=Antiepileptic Drugs.

Programming Note: Use the shell for 14.1.4.4.2 for

Table 14.1.4.4.2
Frequency Distribution for Number of Concomitant Antiepileptic Drugs
Safety Population (Japan)

Table 14.1.5.1
Duration of Treatment Exposure
Safety Population

Time on Treatment (days)	Gp1 (N = XX)	Gp8 (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
n	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
Min	XX	XX	XX	XX
Q1	XX	XX	XX	XX
Q2 (Median)	XX.X	XX.X	XX.X	XX.X
Q3	XX	XX	XX	XX
Max	XX	XX	XX	XX

SD: Standard Deviation. Q1=Lower Quartile; Q2=Median; Q3=Upper Quartile.
Note: Time on treatment (in days) will be calculated per subject as the number of days with IMP intake during the trial. This will be calculated as Date of last IMP intake – Date of first IMP intake + 1.

Programming Note: Use the shell for 14.1.5.1 for

Table 14.1.5.1.3
Duration of Treatment Exposure
Safety Population (Japan)

Table 14.1.5.1.1
Duration of Treatment Exposure by Age Group
Safety Population

	Subjects <6 years at Entry in Core Study (N=xxx)	Subjects ≥6 years at Entry in Core Study (N=xxx)	ALL ZX008 Treated Subjects (N=xx)
Summary Stats			
n	XX	XX	XX
Mean (days)	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Duration of Exposure			
<1 month	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 to <3 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 to <6 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6 to <12 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
12 to <18 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
18 to <24 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
24 to <30 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
30 to <36 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥36 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: De novo subjects are not included in this update. Duration of exposure is calculated from date of first dose in this study to the last date of treatment or data cutoff date for this report, whichever is earlier.

Programming note:

Similar to DX21 in ISS, but population here is the 1503 safety population, and the duration is from day 1 in OLE study; add rows for 24-30 and 30-36 as show in shell

You may present two tables using by group of Age Group or present as above, whichever works best for programming.

Programming note: Use the shell for 14.1.5.1 for

Table 14.1.5.1.4
Duration of Treatment Exposure by Age Group
Safety Population (Japan)

Table 14.1.5.1.2
Duration of Treatment Exposure by Sex
Safety Population

	Female Subjects	Male Subjects	ALL ZX008 Treated Subjects
Summary Stats			
n	XX	XX	XX
Mean (days)	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min, Max	XX, XX	XX, XX	XX, XX
Duration of Exposure			
<1 month	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1 to <3 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3 to <6 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6 to <12 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
12 to <18 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
18 to <24 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
24 to <30 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
30 to <36 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
≥36 months	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Duration of exposure is calculated from date of first dose in this study to the last date of treatment or data cutoff date for this report, whichever is earlier

Programming note:
Similar to DX22 in ISS, but add rows for 24-30, 30-36;

Programming note: Use the shell for 14.1.5.2 for

Table 14.1.5.1.5
Duration of Treatment Exposure by Sex
Safety Population (Japan)

Table 14.1.5.1.6
Duration of Treatment Exposure in ZX008-1502 and ZX008-1503 Combined
Subjects Treated in ZX008-1502 and ZX008-1503 Combined (Japan)

Time on Treatment (days)	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	All Subjects (N = XX)
n	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Min	XX	XX	XX	XX	XX
Q1	XX	XX	XX	XX	XX
Q2 (Median)	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX

SD: Standard Deviation. Q1=Lower Quartile; Q2 = Median; Q3=Upper Quartile
Note: Time on treatment (in days) will be calculated per subject as the number of days with IMP intake during the trial. This will be calculated as Date of last IMP intake in ZX008-1502 or ZX008-1503 – Date of first IMP intake in ZX008-1503 + 1. The duration includes the transition period in ZX008-1502.

Table 14.1.5.1.7.1
Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit
Safety Population

Visit	Last Assigned Dose Prior to Visit	Number of Subjects	Subject dosage (mg/kg) assigned at Visit					
			0.2 mg/kg/day	0.3 mg/kg/day	0.4 mg/kg/day	0.5 mg/kg/day	0.6 mg/kg/day	0.8 mg/kg/day
Visit 2 – Day 15	Subjects attending Visit	XXX						
	0.2 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.3 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.4 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.5 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.6 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.8 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Visit 3 – Month 1	Subjects attending Visit	xxx						
	0.2 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.3 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.4 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.5 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.6 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
	0.8 mg/kg/day		XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

Note: For each visit after Visit 1, the number of subjects who attended the visit is presented. The assigned dosage of ZX008 that the subject was on prior to that visit is provided in the row and the assigned dosage at the conclusion of the visit is provided in the columns. Percentages are based on the number of subjects who attended the visit.

Programming Notes: This table was MAA34 in the ISS package. Continue for other scheduled visits in 1503 through Month 36. Use the Table 14.1.5.1.7.1 shell for

Table 14.1.5.1.7.2
Shift in Assigned ZX008 Dosage in ZX008-1503 by Study Visit
Safety Population (Japan)

Table 14.1.5.8.1
Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment
Safety Population

Duration (Months)	Number of Subjects[2] Receiving ZX008					
	Mean Dose (mg/kg)[1]				Any Dose	
	>0 to 0.2 (n)	>0.2 to 0.4 (n)	>0.4 to 0.6 (n)	>0.6 to 0.8 (n)	Total(N)	(%)
≤1	XX	XX	XX	XX	XX	XX.X
>1 to ≤2	XX	XX	XX	XX	XX	XX.X
>2 to ≤3	XX	XX	XX	XX	XX	XX.X
>3 to ≤4	XX	XX	XX	XX	XX	XX.X
>4 to ≤5	XX	XX	XX	XX	XX	XX.X
>5 to ≤6	XX	XX	XX	XX	XX	XX.X
>6 to ≤7	XX	XX	XX	XX	XX	XX.X
>7 to ≤8	XX	XX	XX	XX	XX	XX.X
>8 to ≤9	XX	XX	XX	XX	XX	XX.X
>9 to ≤10	XX	XX	XX	XX	XX	XX.X
>10 to ≤11	XX	XX	XX	XX	XX	XX.X
>11 to ≤12	XX	XX	XX	XX	XX	XX.X
>12 to ≤18	XX	XX	XX	XX	XX	XX.X
>18 to ≤24	XX	XX	XX	XX	XX	XX.X
>24 to ≤30	XX	XX	XX	XX	XX	XX.X
>30 to ≤36	XX	XX	XX	XX	XX	XX.X
>36 to ≤42	XX	XX	XX	XX	XX	XX.X
>42 to ≤48	XX	XX	XX	XX	XX	XX.X
Total (Any Duration)	XX	XX	XX	XX	XX	XX.X
%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

(%): (n/N) * 100 n: Number in each dosage group. N: total number for the month

[1] The mean daily dose is calculated over a subject's entire treatment period in the trial.

[2] The tabulated frequency in a given cell is the number of subjects whose exposure duration is in that row, and whose mean daily dose over the entire treatment period falls in the specified column. The duration endpoints, in days, are 30, 60, 90, 120, … , 330, 360; for example, a subject exposed for 70 days will be counted in the >2 to ≤3 months row. The mean daily dose is then calculated for each subject for dose categorization. For example, if the above subject had a mean daily dose of 0.7 mg/kg during 70 days of exposure, that subject will be counted in the >0.6 to 0.8 mg/kg column.

Programming Note: This table is calculated by first categorizing subjects on the basis of the interval of exposure for each (e.g., a subject exposed for 6 and a half months would be counted in the >6 to ≤7 row. The mean daily dose is then calculated for each subject for dose categorization (e.g., a subject with a mean daily dose of 0.5 mg/kg would be counted in the >0.4 to 0.6 column). Subjects are enumerated in only 1 cell of the matrix (i.e., this is a mutually exclusive display). Mean doses in the >4 to ≤5 row refer to mean doses over 0-5 months, not month 4-5.

Programming Note: Use the same shell for Table 14.1.5.1.8.1 shell for

Table 14.1.5.8.2
Number of Subjects Receiving ZX008 According to Mean Daily Dose and Duration of Treatment
Safety Population (Japan)

Table 14.1.5.1.9.1
Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment
Safety Population

Duration (Months)	Number of Subjects[2] Receiving ZX008					
	Mean Dose (mg/day) [1]				Any Dose	
	< 5 (n)	5 - <10 (n)	10 - < 20 (n)	20 – 30 (n)	Total(N)	(%)
≤1	XX	XX	XX	XX	XX	XX.X
>1 to ≤2	XX	XX	XX	XX	XX	XX.X
>2 to ≤3	XX	XX	XX	XX	XX	XX.X
>3 to ≤4	XX	XX	XX	XX	XX	XX.X
>4 to ≤5	XX	XX	XX	XX	XX	XX.X
>5 to ≤6	XX	XX	XX	XX	XX	XX.X
>6 to ≤7	XX	XX	XX	XX	XX	XX.X
>7 to ≤8	XX	XX	XX	XX	XX	XX.X
>8 to ≤9	XX	XX	XX	XX	XX	XX.X
>9 to ≤10	XX	XX	XX	XX	XX	XX.X
>10 to ≤11	XX	XX	XX	XX	XX	XX.X
>11 to ≤12	XX	XX	XX	XX	XX	XX.X
>12 to ≤18	XX	XX	XX	XX	XX	XX.X
>18 to ≤24	XX	XX	XX	XX	XX	XX.X
>24 to ≤30	XX	XX	XX	XX	XX	XX.X
>30 to ≤36	XX	XX	XX	XX	XX	XX.X
>36 to ≤42	XX	XX	XX	XX	XX	XX.X
>42 to ≤48	XX	XX	XX	XX	XX	XX.X
Total (Any Duration)	XX	XX	XX	XX	XX	XX.X
%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

(%): (n/N) * 100 n: Number in each dosage group. N: total number for the month

[1] The mean daily dose is calculated over a subject's entire treatment period in the trial.

[2] The tabulated frequency in a given cell is the number of subjects whose exposure duration is in that row, and whose mean daily dose over the entire treatment period falls in the specified column. The duration endpoints, in days, are 30, 60, 90, 120, … , 330, 360. For example, a subject exposed for 70 days will be counted in the >2 to <=3 months row. The mean daily dose, in mg/day, is then calculated for each subject for dose categorization.

Programming Note: See MAA Table 14.1.5.3 \120_mg_day.
Use the same shell for Table 14.1.5.1.9.1. shell for

Table 14.1.5.1.9.2
Number of Subjects Receiving ZX008 According to Mean Dose (mg/day) and Duration of Treatment
Safety Population (Japan)

Table 14.1.5.1.10.1
Number of Subjects Receiving ZX008 According to Actual Daily Dose (mg/kg) and Duration of Treatment
Safety Population

Duration (Months)	Number of Subjects[2] Receiving ZX008					
	Actual Daily Dose (mg/kg) [1]				Any Dose	
	>0 to 0.2 (n)	>0.2 to 0.4 (n)	>0.4 to 0.6 (n)	>0.6 to 0.8 (n)	Total(N)	(%)
≤1	XX	XX	XX	XX	XX	XX.X
>1 to ≤2	XX	XX	XX	XX	XX	XX.X
>2 to ≤3	XX	XX	XX	XX	XX	XX.X
>3 to ≤4	XX	XX	XX	XX	XX	XX.X
>4 to ≤5	XX	XX	XX	XX	XX	XX.X
>5 to ≤6	XX	XX	XX	XX	XX	XX.X
>6 to ≤7	XX	XX	XX	XX	XX	XX.X
>7 to ≤8	XX	XX	XX	XX	XX	XX.X
>8 to ≤9	XX	XX	XX	XX	XX	XX.X
>9 to ≤10	XX	XX	XX	XX	XX	XX.X
>10 to ≤11	XX	XX	XX	XX	XX	XX.X
>11 to ≤12	XX	XX	XX	XX	XX	XX.X
>12 to ≤18	XX	XX	XX	XX	XX	XX.X
>18 to ≤24	XX	XX	XX	XX	XX	XX.X
>24 to ≤30	XX	XX	XX	XX	XX	XX.X
>30 to ≤36	XX	XX	XX	XX	XX	XX.X
>36 to ≤42	XX	XX	XX	XX	XX	XX.X
>42 to ≤48	XX	XX	XX	XX	XX	XX.X
Total (Any Duration)	XX	XX	XX	XX	XX	XX.X
%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

(%): (n/N) * 100 n: Number in each dosage group. N: total number for the month

[1] The actual dosage in mg/day assigned by the investigator over the course of the study..

[2] The times on a particular dosate may not be concurent. The tabulated frequency in a given cell is the number of subjects whose exposure duration is in that row, and whose assigned dosage over the entire treatment period falls in the specified column. The duration endpoints, in days, are 30, 60, 90, 120, … , 330, 360;

Programming Note: Use the same shell for Table 14.1.5.1.10.1. shell for

Table 14.1.5.1.10.2
Number of Subjects Receiving ZX008 According to Actual Dose (mg/day) and Duration of Treatment
Safety Population (Japan)

Table 14.1.5.2.1
Compliance to IMP intake
Safety Population

	Gp1 (N = XX)	Gp8 (N = xx)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Overall compliance % during OLE Treatment Period				
N	XX	XX	XX	XX
Mean	XX.XX	XX.XX	XX.XX	XX.XX
SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX
Median	XX.XX	XX.XX	XX.XX	XX.XX
Min	XX.X	XX.X	XX.X	XX.X
Max	XX.X	XX.X	XX.X	XX.X
Compliance category				
<80%	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
80-<90%	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
90-<100%	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
100-<110%	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
>110%	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

IMP = Investigational medicinal product; OL=Open-label; OLE=Open-label Extension.
Note: Percentages are calculated based on the number of subjects with non-missing data in the Safety population.

Programming Note: For each day, based on the response to the daily diary, a missed dose=0% of dose consumed, partial=50% of dose consumed, and full=100% of dose consumed. For each subject, a daily compliance score will be thus obtained. The total score for the subject during the study will then be divided by the number of days on study and multiplied by 100.

Programming note: use table shell for 14.1.5.2.1 for the production of

Table 14.1.5.2.1.1
Compliance to IMP intake
Safety Population (Japan)

Table 14.1.5.2.2
Compliance to IMP intake
mITT Population

Table 14.1.5.2.2.1
Compliance to IMP intake
mITT Population (Japan)

Table 14.2.1.1.1
Convulsive seizure frequency per 28 days during Baseline (Core), Double-blind and OLE Treatment Period:
Summary statistics and Tests of Changes from Baseline
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	All treatments combined* (N = XX)	De Novo Subjects (N = XX) **
Baseline[1]						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) [2]						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study Final Week of T+M [3]						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	All treatments combined* (N = XX)	De Novo Subjects (N = XX) **
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study Final Week of T+M Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study Final Week of T+M % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month1 (OLE)						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month1 (OLE) Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month1 (OLE) % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	All treatments combined* (N = XX)	De Novo Subjects (N = XX) **
Month2 (OLE)						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month2 (OLE) Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month2 (OLE) % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
……						
Repeat for Month3, Month4-6, Month7-9, Month10-12, Month13-15, Month16-18, Month19-21, Month22-24, Month 25-27, Month 28-30, Month 31-33, Month 34-36						
ENDPOINT1: Overall OLE Treatment Period						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT1: Overall OLE Treatment Period Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	All treatments combined* (N = XX)	De Novo Subjects (N = XX) **
ENDPOINT1: Overall OLE Treatment Period % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
ENDPOINT2: Month02-EOS						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT2: Month02-EOS Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT2: Month02-EOS % Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX

*Includes subjects randomizedto placebo and all doses of ZX008 during DB.

** For De Novo subjects, the baseline period is the 28 days prior to dosing in ZX008-1503. Change from baseline for this group is calculated relative to this baseline period.

T+M = Titration + Maintenance; OLE = Open-label extension; SD = Standard deviation; Chg = Change; EOS = End of study

Data from core study includes subjects on Placebo as well as ZX008.

[1] Baseline=Baseline prior to double-blind treatment in the core study or 28 days prior to dosing in ZX008-1503 for De Novo Subjects. Subjects in 1504-C1 do not have a Baseline(Core).

[2] Core Study (T+M) is the entire Titration+Maintenance Period during the Core study; does not include the transition period.

[3] Core Study Final Week of T+M is the last 7 days of the T+M period.
[4]P-value for within group % change from baseline is based on Wilcoxon signed rank test that the % change from baseline is statistically significantly different from 0.
Programming note:

P-values are only calculated for the OLE Period, starting from Month1 onward. The p-value will be obtained for the percentage change from baseline, not the change from baseline. Please see SAP section 6.1.6. It does does matter whether we attach the p-value to the change stats or the percent change stats; Zogenix wantsthe p-value from the analysis of the percentage changes from baseline. Use the round function to get the percentage change to 3 or 4 decimal places before calculating pccs25yn, pccs50yn, pccs75yn and especially pccs00yn.]

Code to get p-value for percentage change at each time point:: calculate the percentage change from baseline:
For example:

```
Data temp;
 Set data1;
 if base ne . and twval ne .;
chng = base – twval;
pctchng=(base – twval)/base;
run;

ods trace on;
ods output TestsForLocation=univout;
proc univariate data=anal;
  var pctchng;
 run;
ods trace off;

 data dpout;
  set univout;
  where Test='Signed Rank' and Testlab='S';
  pout=pValue;  **be sure to write "<0.001" if the p-value is <0.001;
  keep pctchng Test pout;
 run;
```

Programming Note: Use the same 14.2.1.1.1 shell for

Table 14.2 1.1.6
Convulsive seizure frequency per 28 days during Baseline (Core), Double-blind and OLE Treatment Period:
Summary statistics and Tests of Changes from Baseline
mITT Population (Japan)

Programming Note: Use the shell for 14.2.1.1.1 to produce:

Table 14.2.1.1.2
Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group:
Summary statistics and Tests of Changes from Baseline
mITT Population

Table 14.2.1.1.7
Convulsive seizure frequency per 28 days during OLE Treatment Period, by Age Group:
Summary statistics and Tests of Changes from Baseline
mITT Population (Japan)

Programming Note: Add Header, top left, prior to the table proper, "Age Group: <6 years" or "Age Group: >= 6 years"

Table 14.2.1.1.3
Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary Statistics and Tests of Changes from Baseline
mITT Population

	ZX008 Low Mean Daily Dose* (>0 - <0.4 mg/kg) (N = XX)	ZX008 Medium Mean Daily Dose* (0.4 – 0.6 mg/kg) (N = XX)	ZX008 High Mean Daily Dose* (>0.6 mg/kg) (N = XX)	Any ZX008 OL Dose* (N = XX)
Baseline[1]				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) [2]				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study (T+M) % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study Final Week of T+M [3]				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

	ZX008 Low Mean Daily Dose* (>0 - <0.4 mg/kg) (N = XX)	ZX008 Medium Mean Daily Dose* (0.4 – 0.6 mg/kg) (N = XX)	ZX008 High Mean Daily Dose* (>0.6 mg/kg) (N = XX)	Any ZX008 OL Dose* (N = XX)
Core Study Final Week of T+M Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Core Study Final Week of T+M % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month 1 (OLE)				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month 1 (OLE) Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX
Month 1 (OLE) % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX

	ZX008 Low Mean Daily Dose* (>0 - <0.4 mg/kg) (N = XX)	ZX008 Medium Mean Daily Dose* (0.4 – 0.6 mg/kg) (N = XX)	ZX008 High Mean Daily Dose* (>0.6 mg/kg) (N = XX)	Any ZX008 OL Dose* (N = XX)
Month 2 (OLE)				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month 2 (OLE) Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Month2 (OLE) % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX
……				
Repeat for Month3, Month6, Month9, Month12, Month15, Month18, Month21, Month24				
ENDPOINT1: Overall OLE Treatment Period				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT1: Overall OLE Treatment Period Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

	ZX008 Low Mean Daily Dose* (>0 - <0.4 mg/kg) (N = XX)	ZX008 Medium Mean Daily Dose* (0.4 – 0.6 mg/kg) (N = XX)	ZX008 High Mean Daily Dose* (>0.6 mg/kg) (N = XX)	Any ZX008 OL Dose* (N = XX)
ENDPOINT1: Overall OLE Treatment Period % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX
ENDPOINT2: Month02-EOS				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT2: Month02-EOS Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
ENDPOINT2: Month02-EOS % Change from Baseline				
N	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX

T+M = Titration + Maintenance; OLE = Open-label extension; SD = Standard deviation; Chg = Change; EOS = End of study

Data from core study includes subjects on Placebo as well as ZX008

*Note: The calculated (weight adjusted) daily doses over the entire OLE period were averaged to get a mean dialy dose, which was then categorized as follows: > 0 – <0.4 mg/kg = Low; 0.4 – 0.6 mg/kg = Medium; >0.6 mg/kg = High

[1] Baseline=For subjects who participated in a doube-blind study, the Baseline prior to double-blind treatment in the core study. Subjects in 1504-C1 do not have a Baseline(Core), and are not included in this table. For De Novo subjects, the baseline period is the 28 days prior to dosing in ZX008-1503. Change from baseline for this group is calculated relative to this baseline period.
[2] Core Study is the entire Titration+Maintenance Period during the Core study; does not include the transition period.
[3] Core Study Final Week of T+M is the last 7 days of the T+M period.
[4]P-value for within group change from baseline is based on Wilcoxon signed rank test that the change from baseline is statistically significantly different from 0.

Programming note: Need to use exposure data to determine mean daily dose during OLE for each subject, and categorize each subject as having had Low, Medium or High dose of ZX008 as follows:

0 – <0.4 mg/kg = Low; 0.4 – 0.6 mg/kg = Medium; >0.6 mg/kg = High

Programming note: Use the shell for Table 14.2.1.1.3 for

Table 14.2.1.1.8
Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose: Summary Statistics and Tests of Changes from Baseline
mITT Population (Japan)

Table 14.2.1.1.4
Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, by Age Group: Summary Statistics and Tests of Changes from Baseline
mITT Population

Programming Note: Repeat 14.2.1.1.3 for Age groups <6, and ≥6.

Add Header, top left, prior to the table proper, “Age Group: <6 years” or “Age Group: >= 6 years”.

Programming Note: Use the same shell fo produce

Table 14.2.1.1.9
Convulsive seizure frequency per 28 days during OLE Treatment Period Using Mean Daily Dose, by Age Group: Summary Statistics and Tests of Changes from Baseline
mITT Population (Japan)

Table 14.2.1.1.5
Convulsive seizure frequency per 28 days during OLE Treatment Period: Summary Statistics
Subjects from 1504 Cohort 1

	ZX008 OL[1] (N = XX)
Core Study Day 2 through End of PK Follow-up Period *	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X
Core Study Transition Period**	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X
Month1 (OLE)	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X
Month2 (OLE)	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X
……	
Repeat for Month3, Month6, Month9, Month12, Month15, Month18, Month21, Month24, Month 27, Month 30, Month 33, Month 36	
ENDPOINT1: Overall OLE Treatment Period	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X

	ZX008 OL[1] (N = XX)
ENDPOINT2: Month02-EOS	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX.X, XX.X

Notes:

[1]Subjects were on open-label ZX008 0.2 mg/kg during the entire 6 months of the Transition Period. Starting from Day 1 in the OLE Period, their dose was set at 0.2 mg/kg for the first month, and subsequently adjusted by the PI to achieve optimal dose for effectiveness/tolerability.

*For most subjects this ends on Day 15; for some subjects the PK Period ends on Day 14 or Day 16.

**Transition Period starts 1 day after end of PK Follow-up Period and ends 1 day prior to OLE Visit 1 Day 1.

Table 14.2.1.2
Convulsive seizure frequency per 28 days - ENDPOINT: Parametric Analysis
mITT Population

Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)
ENDPOINT1: OLE TREATMENT PERIOD ANALYSIS					
Baseline (Core) Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Core Study Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
OLE Period Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
OLE Period: Parametric Model Summary[1]					
Results on log scale[2]					
Least Squares Mean (SE) [2]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	

Original scale					
Least Squares Mean[3]	XX.X	XX.X	XX.X	XX.X	
95% CI[3]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	
ENDPOINT2: MONTH2 TO EOS ANALYSIS					
Baseline (Core) Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Core Study Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Month2 to EOS Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Month2 to EOS: Parametric Model Summary[1]					
Results on log scale[2]					
Least Squares Mean (SE) [2]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	
Original scale					
Least Squares Mean[3]	XX.X	XX.X	XX.X	XX.X	
95% CI[3]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	

mITT = Modified intent-to-treat population; CI = Confidence Interval; SD = Standard Deviation; SE = Standard Error.
Note: this table excludes de Novo subjects.
[1] Baseline and overall OLE values were log transformed prior to analysis. To avoid taking log of 0, a value of 1 was added to each subject's convulsive seizure frequency value (with the exception of the Baseline (Core) value) before log transformation.
[2] Results are based on an ANCOVA model with treatment group (four levels excluding group that contained all subjects enrolled in 1503 – regardless of feeder study) and age group (< 6 years, ≥6 years) as factors, log baseline convulsive seizure frequency as a covariate, CSF during Core Study as another covariate, and log convulsive seizure frequency (overall OLE period, or Month2 to EOS) as response.
[3]Values obtained from the ANCOVA model were exponentiated to get the corresponding values on the original scale.

Programming note: Use PROC MEANS for summary stats, and PROC GLM for parametric model analysis.

Table 14.2.1.3
Convulsive seizure frequency per 28 days - ENDPOINT: Nonparametric Analysis
mITT Population

Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)
ENDPOINT1: OLE TREATMENT PERIOD ANALYSIS					
Baseline (Core) Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Core Study Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
OLE Period Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
OLE Period: Nonparametric Model Summary[1]					
Results on rank scale					
Least Squares Mean (SE) [2]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	

Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)
MONTH2 to EOS ANALYSIS					
Baseline (Core) Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Core Study Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Month2 to EOS Ranks[1]: Summary Statistics					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Month2 to EOS Analysis: Nonparametric Model Summary[1]					
Results on rank scale					
Least Squares Mean (SE) [2]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	

mITT = Modified intent-to-treat population; CI = Confidence Interval; SD = Standard Deviation; SE = Standard Error.
Note: this table excludes de Novo subjects.
[1] Baseline, Core Study, Month3 to EOS and overall OLE values were rank transformed prior to analysis.

[2]The results are on the rank scale. Results are based on an ANCOVA model with treatment group (four levels excluding group that contained all subjects enrolled in 1503 – regardless of feeder study) and age group (< 6 years, ≥6 years) as factors, rank of baseline convulsive seizure frequency as a covariate, rank of Core Study CSF as another covariate, and rank of convulsive seizure frequency (overall OLE period, or Month2 to EOS) as response.

Programming note: Rank the baseline and OLE period convulsive seizure frequency, then use PROC MEANS for summary stats, and PROC GLM for parametric model analysis. See stats manual.

Table 14.2.1.4
Convulsive seizure frequency per 28 days, Over Time – Parametric Analysis
mITT Population

Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)
SUMMARY STATISTICS					
Baseline (Core)					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
Core Study					
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX
RESULTS FROM GENERAL LINEAR MODEL					
Month1: Parametric Model Summary					
Results on log scale[1]					
Least Squares Mean (SE) [1]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [1]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	
Original scale					
Least Squares Mean[2]	XX.X	XX.X	XX.X	XX.X	
95% CI[2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	

…. (Repeat for months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, and 36

mITT = Modified intent-to-treat population; CI = Confidence Interval; SD = Standard Deviation; SE = Standard Error.
Note: this table excludes de Novo subjects.
[1] Baseline and overall OLE values were log transformed prior to analysis. To avoid taking log of 0, a value of 1 was added to each subject's convulsive seizure frequency value (the response variable) for each timepoint in the OLE period before taking the natural logarithm.
[2] Results are based on a general linear model with fixed effects for treatment group (four levels excluding group that contained all subjects enrolled in 1503 – regardless of feeder study) and age group (< 6 years, ≥6 years), time (Months 1, 2, 3, 6, 9, 12, 15, 18, 21,and 24) and log baseline convulsive seizure frequency as a covariate; and random effects for subject (repeated over time). The dependent variable is log convulsive seizure frequency (overall OLE period) as response.
[3] Values obtained from the ANCOVA model were exponentiated to get the corresponding values on the original scale.

Programming note: Use PROC MEANS for summary stats
For MMRM model, use PROC MIXED. Before calling the PROC, please add 1 to the Month1, Month2, … Month24 CSF values, then take the natural log (log to base e) of these values to be used in the model. PROC MMRM for parametric model analysis. The LSMeans are the LSMeans for the time*treatment interaction terms. See stats manual.

Programming Notes: Use the shell for 14.2.1.4 for

Table 14.2.1.5
Convulsive seizure frequency per 28 days, Over Time – Parametric Analysis Using Mean Daily Dose
mITT Population

In place of treatment groups, categorize subjects into three treatments depending on their mean daily dose during the OLE Treatment period as Low, Medium, and High. See SAP.

Categories for Low, Medium, High depending on the following doses of ZX008

<0.4 mg/kg = Low
0.4-0.6 mg/kg = Medium
>0.6 mg/kg = High

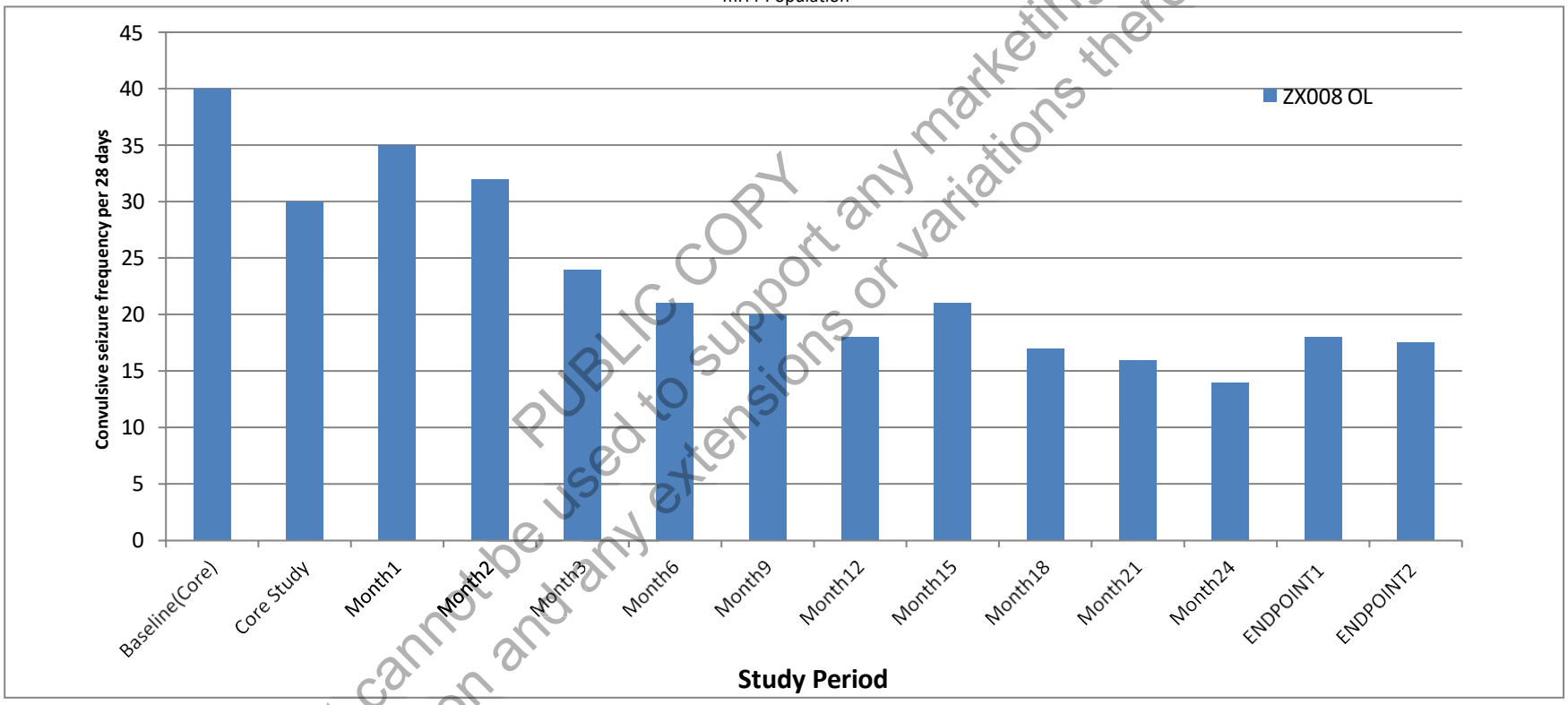
Table 14.2.1.6
% of Subjects with Changes in AED medications during 1st 6 months of OLE Treatment Period
mITT Population

OLE Period	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)
Any Change in AED medication during the 1st 6 months	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 1	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 2	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 3	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 4	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 5	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Month 6	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

mITT = Modified intent-to-treat population ; Months are defined in 30 day increments. Month1=Day1-Day30, Month2=Day31-Day60, and so on.

Programming Note: we need to determine what a change in AED medication is

Figure 14.2.1.7
Graph of means for convulsive seizure frequency per 28 days during OLE Treatment Period
mITT Population



mITT = Modified intent-to-treat population

Programming Note: This plots the means from Table 14.2.1.1.1

Figure 14.2.1.8
Graph of model adjusted means for Convulsive seizure frequency per 28 days – mITT Population

Programming note: Forest plots for the model adjusted means and CIs

Programming note: Repeat Figure 14.2.1.7 using the following 3 treatment groups: Low, Medium, and High to produce

Figure 14.2.1.9
Graph of convulsive frequency per 28 days, Over Time, Using Mean Daily Dose
mITT Population

Table 14.2.2.1
Percent Reduction in Convulsive Seizure Frequency, OLE Treatment Period
mITT Population

Time Period	Distribution of Percentage Change from Baseline(Core) in convulsive Seizure Frequency[1]	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL # (N = XXX)	De Novo Subjects (N = XXX)
OLE Period	≥25%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	≥50%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	≥75%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	=100%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
Month 1	≥25%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	≥50%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	≥75%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%
	=100%: n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	95%CI*	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%	XX.X%, XX.X%

mITT = Modified Intent-to treat; CI = Confidence Interval; *Exact Clopper-Pearson CI. # Excludes the De Novo subjects.

[1]Baseline=Baseline prior to double-blind treatment in the core study. Subjects in 1504-C1 do not have a Baseline(Core), and are not included in this table.

Programming Note: …. Repeat for months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, and 36. Use the Table 14.2.2.1 shell for

Table 14.2.2.1.1
Percent Reduction in Convulsive Seizure Frequency, OLE Treatment Period
mITT Population (Japan)

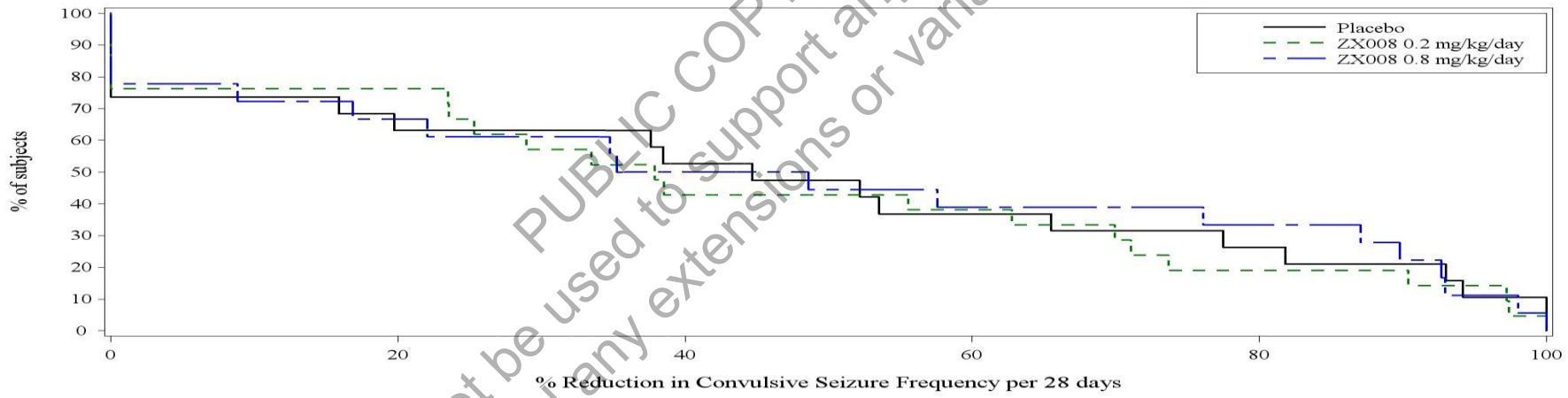
Figure 14.2.2.2
Cumulative Response Curves for Percent Reduction in CSF during OLE Treatment Period
mITT Population

Example graph: From PROC LIFETEST.

Zogenix Inc.
Protocol: ZX008-VS01

Page 1 of 1

Figure A14.2.2.2.1
Cumulative Response Curve for % reduction in seizure frequency per 28 days
mITT Population



Program: rgkmtest_strpntl.sas Output: FA14_02_02_02_01.rtf Date: 06APR2018 15:45

Example graph above: use rgkmtest_strpntl.sas

Programming Note: Use the Figure 14.2.2.2 shell for

Figure 14.2.2.2.1
Cumulative Response Curves for Percent Reduction in CSF during OLE Treatment Period
mITT Population (Japan).

Footnote: mITT = Modified intent-to-treat population.

Table 14.2.3.1
Duration of the Longest interval (days) between convulsive seizures
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
n	XX	XX	XX	XX	XX	XX
mean	XX.x	XX.x	XX.x	XX.x	XX.x	XX.x
SD	XX.xx	XX.xx	XX.xx	XX.xx	XX.xx	XX.xx
Min	XX	XX	XX	XX	XX	XX
25th Percentile	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
75th Percentile	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Max	XX	XX	XX	XX	XX	XX

mITT = Modified Intent-to-treat; CI = Confidence Interval;
Note: Percentages are calculated based on the number of subjects with non-missing data in the modified ITT population.

Figure 14.2.3.2
Boxplot of Distribution of Duration of Longest Interval between Convulsive Seizures during OLE Treatment Period
mITT Population

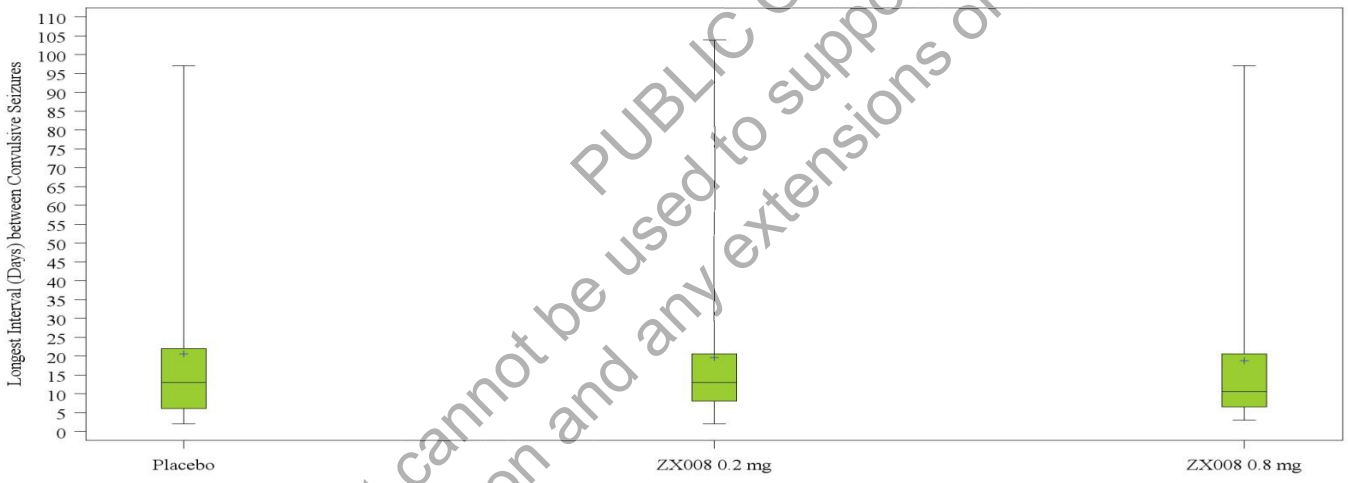
Programming notes:
Footnote: mITT = Modified intent-to-treat population

Example only: Separate boxplot for each group.
For interim analysis, if done, use only one box, for Group 9 (ZX008 OL, All Subjects)

Zogenix Inc.
Protocol: ZX008-VS01

Page 1 of 1

Figure 14.2.3.2 - Boxplot of distribution of longest interval between convulsive seizures
mITT Population



Program: rgfreq.sas Output: F14_02_03_02.rtf

10NOV2017 18:32

Table 14.2.4.1
Summary of Duration of Convulsive Seizure Episodes during OLE Treatment Period
mITT Population

Convulsive Seizure Duration	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Total no. with at least one episode[1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Total no. of episodes	XXX	XXX	XXX	XXX	XXX	XXX
< 2-minute duration						
No. of subjects	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No. of episodes	XXX	XXX	XXX	XXX	XXX	XXX
2 – 10-minute duration						
No. of subjects	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
No. of episodes	XXX	XXX	XXX	XXX	XXX	XXX
>10 minutes duration						XX (XX.X%)
No. of subjects	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XXX
No. of episodes	XXX	XXX	XXX	XXX	XXX	
Clusters of Convulsive Seizures						XX (XX.X%)
No. of subjects	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XXX
No. of episodes	XXX	XXX	XXX	XXX	XXX	

mITT = Modified Intent-to-treat; % = n/N*100 where n is number in category and N is number in cohort(except Total Recurring Seizures)
[1] % = ((Number in Cohort)/(Grand Total))*100.

Table 14.2.4.2
Summary of Gaps between Convulsive Seizure Episodes during OLE Treatment Period
mITT Population

Duration by Number of Days* between Convulsive Seizure Episodes	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
1 Recurrence						
n	XX	XX	XX	XX	XX	XX
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
2 Recurrences	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
3 Recurrences	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
4 Recurrences	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
>= 5 Recurrences	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX

mITT = Modified Intent-to-treat; % = n/N*100 where n is number in category and N is number in cohort(except Total Recurring Seizures)
*A Recurrence day is a day on which a subject has a seizure, given that the subject has had a seizure on another day previously.

Programming Note: Use shell for Table 14.2.1.1.1 to produce

Table 14.2.5.1
Convulsive seizure-free days – summary statistics
mITT Population
Note: Percentage of convulsive seizure free days will be calculated as the total of seizure free days / total number of days with non-missing diary data*100.

Table 14.2.5.2
Convulsive seizure-free days - Parametric Analysis - MMRM by Age Group
mITT Population

Statistics	Age < 6 years (N = XX)	Age >= 6 years (N = XX)	ZX008 OL (N = XX)
SUMMARY STATISTICS			
Baseline (Core)			
N	XX	XX	XX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min	XX	XX	XX
Max	XX	XX	XX
Core Study			
N	XX	XX	XX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min	XX	XX	XX
Max	XX	XX	XX
Month 1 (Original Scale) Summary Statistics			
N	XX	XX	XX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min	XX	XX	XX
Max	XX	XX	XX
RESULTS FROM MMRM MODEL			
Results on log scale[1]			
Least Squares Mean (SE) [1]	XX.X (XX.XX)	XX.X (XX.XX)	
95% CI for Least Squares Mean [1]	(XX.X,XX.X)	(XX.X,XX.X)	

Original scale		
Least Squares Mean[2]	XX.X	XX.X
95% CI[2]	(XX.X,XX.X)	(XX.X,XX.X)

…. (Repeat for months 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, and 36.

mITT = Modified intent-to-treat population; CI = Confidence Interval; SD = Standard Deviation; SE = Standard Error. MMRM = Mixed Model Repeated Measures.

[1] Baseline and overall OLE values were log transformed prior to analysis. Results are scaled to the number of seizure free days per 28 days. To avoid taking log of 0, a value of 1 was added to each subject's convulsive seizure frequency value (the response variable) for each timepoint in the OLE period before taking the natural logarithm.

[2]Results are based on a MMRM with fixed effects for age group (< 6 years, ≥6 years), time (Months 1, 2, 3, 6, 9, 12, 15, 18, 21,and 24), and log baseline convulsive seizure-free days and log T+M seizure free days as covariates; and random effects for subject (repeated over time). The dependent variable is log convulsive seizure-ree fdays / 28 days frequency.

[3]Values obtained from the MMRM model were exponentiated to get the corresponding values on the original scale.

Table 14.2.5.3
Convulsive seizure-free days - Parametric Analysis - MMRM by Mean Daily Dose
mITT Population

Statistics	ZX008 Low Mean Daily Dose* (>0 - <0.4 mg/kg) (N = XX)	ZX008 Medium Mean Daily Dose* (0.4 – 0.6 mg/kg) (N = XX)	ZX008 High Mean Daily Dose* (>0.6 mg/kg) (N = XX)	Any ZX008 OL Dose* (N = XX)
SUMMARY STATISTICS				
Baseline (Core)				
N	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX
Max	XX	XX	XX	XX
Core Study				
N	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX
Max	XX	XX	XX	XX
Month 1 (Original Scale) Summary Statistics				
N	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX
Max	XX	XX	XX	XX
RESULTS FROM MMRM MODEL				
Results on log scale[1]				
Least Squares Mean (SE) [1]	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
95% CI for Least Squares Mean [1]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)

Original scale				
Least Squares Mean[2]	XX.X	XX.X	XX.X	XX.X
95% CI[2]	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)

…. (Repeat for months2, 3, 6, 9, 12, 15, 18, 21 and 24

mITT = Modified intent-to-treat population; CI = Confidence Interval; SD = Standard Deviation; SE = Standard Error. MMRM = Mixed Model Repeated Measures.

*Note: The calculated (weight adjusted) daily doses over the entire OLE period were averaged to get a mean dialy dose, which was then categorized as follows: > 0 – <0.4 mg/kg = Low; 0.4 – 0.6 mg/kg = Medium; >0.6 mg/kg = High.

[1] Baseline and overall OLE values were log transformed prior to analysis. Results are scaled to the number of seizure free days per 28 days. To avoid taking log of 0, a value of 1 was added to each subject's convulsive seizure frequency value (the response variable) for each timepoint in the OLE period before taking the natural logarithm.

[2]Results are based on a MMRM with fixed effects for mean daily dose (3 levels), time (Months 1, 2, 3, 6, 9, 12, 15, 18, 21,and 24), and log baseline convulsive seizure-free days and log T+M seizure free days as covariates; and random effects for subject (repeated over time). The dependent variable is log convulsive seizure-ree fdays / 28 days frequency.

[3]Values obtained from the MMRM model were exponentiated to get the corresponding values on the original scale.

Programming Notes: Use shell for Table 14.2.1.5.1 to produce

Table 14.2.5.4
Convulsive seizure-free days – summary statistics for subjects from Study 1504 –Cohort 1

Treatment group is Group 5.
Time periods do not include a Baseline(Core), as cohort 1 subjects did not have the extended baseline period that those in cohort 2 and 1501, 1502 subjects had.

Table 14.2.6.1
Non-convulsive seizure frequency during OLE Treatment Period
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = xx)
Non-convulsive seizure frequency (All types)						
Baseline *						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, xx	XX, xx	XX, XX	XX, XX	XX, XX
OLE Treatment Period						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, xx	XX, xx	XX, XX	XX, XX	XX, XX
Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, xx	XX, xx	XX, XX	XX, XX	XX, XX
P_value**	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
% Change from Baseline						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, xx	XX, xx	XX, XX	XX, XX	XX, XX

Least Squares Mean (SE)***	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)		
95% CI for Least Squares Mean***	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)	(XX.X,XX.X)		

mITT = Modified Intent-to-treat; CI = Confidence Interval; ANCOVA = Analysis of Covariance;

SE = Standard Error.

* Note: The baseline for De Novo subjects is based on the 28 day period prior to dosing in the ZX008-1503 study.

**P-value from the Wilcoxon signed ranks test of the change from baseline being significantly different from 0.

*** Note: Results are based on an ANCOVA model on change from baseline in non-convulsive seizure frequency, with baseline non-convulsive seizure frequency and age as covariates and treatment as a fixed effect. The model excludes the de novo subjects.

Programming note: ***Use the table shell for Table 14.2.6.1 to produce the following tables.***

Table 14.2.6.1.1
Non-convulsive seizure frequency during OLE Treatment Period
mITT Population (Japan)

Table 14.2.6.2
Convulsive + non-convulsive seizure frequency during OLE Treatment Period
mITT Population

Table 14.2.6.2.1
Convulsive + non-convulsive seizure frequency during OLE Treatment Period
mITT Population (Japan)

Table 14.2.7.1
Days with Rescue Medication Usage during the OLE Treatment Period
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Number (%) of Subjects with at Least One rescue medication used during OLE Treatment Period	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
NUMBER OF DAYS RESCUE MEDICATION USED DURING OLE, BY OLE TREATMENT PERIOD						
Number of days rescue medication used per 28 days OLE Month1 [1]						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.XX (XX.XXX)	XX.XX (XX.XXX)	XX.XX (XX.XXX)	XX.XX (XX.XXX)	XX.XX (XX.XXX)	XX.XX (XX.XXX)
Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
…						
Repeat for OLE Months 2 and 3, Month 4-6, Month 9-12, Month 13-15, Month 16-18, Month 19-21, Month 21-24.. etc, Month 33-36.						
Number of days rescue medication used per 28 days during OLE Treatment Period [1]						
N	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, XX	XX, xx	XX, XX	XX, XX	XX, XX

mITT = Modified Intent-to-treat
[1]This is normalized to 28 days.

Programming note: ***"Rescue medications" are those marked in the diary as such. Need to identify these and note usage during the baseline and treatment periods.***

Programming note: Use the Table 14.2.7.1 shell fo produce

Table 14.2.7.2
Days with Rescue Medication Usage during the OLE Treatment Period
mITT Population (Japan)

Table 14.2.8.1
Hospitalization and Other Healthcare Resource Utilization to Treat Seizure
mITT Population

Event or Procedure	PBO-ZX008 OL (N = XX)	ZX 0.2 - ZX008 OL (N = XX)	ZX 0.5 - ZX008 OL (N = XX)	ZX 0.8 - ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
No. (%) of Subjects with at least one hospital admission to treat seizures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Number of Hospital Admissions to treat seizures						
No. of subjects (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Number of occurrences for subjects with at least one						
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx
Occurrences per 100 subject years [1]	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
EEG						
No. of subjects (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Number of occurrences for subjects with at least one						
Mean (SD)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)	XX.X (xx.xx)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min, Max	XX, xx	XX, XX	XX, xx	XX, XX	XX, XX	XX, XX
Occurrences per 100 subject years [1]	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Repeat for the following						
ECG						
ECHO						
PET Scans						
MRI						
X Ray						
CT Scan						

Surgery						
Lumber Puncture / Spinal Tap						
Other						

mITT = Intent-to-treat;
The mean, median, min and max describe the number of events or procedures per subject for those subjects who had at least one event or procedure.
[1] Occurrence rate is based on the total number of occurrences during the study divided by the total number of subject years of followup for subjects in the column. Multiple occurrences for the same subject are included.

Programming note: Use the same Table 14.2.8.1 shell to produce

Table 14.2.8.2
Hospitalization and Other Healthcare Resource Utilization to Treat Seizure
mITT Population (Japan)

Table 14.2.9.1
Number of episodes of status epilepticus (SE)
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.2 - ZX008 OL (N = XX)	ZX 0.5 - ZX008 OL (N = XX)	ZX 0.8 - ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Subjects with at Least One episode of status epilepticus reported as AE[1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of seizures reported greater than 10 min[2]						
No. of subjects	XX	XX	XX	XX	XX	XX
Mean per subject	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Std. Error	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
Total unique events: SE as an AE, plus seizures >10 min						
No. (%) of Subjects with at least one event	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Age group <6 years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% Exact CI	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)
Age group ≥6 years	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% Exact CI	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)	(xx.x%,xx.x%)
Total unique events: SE as an AE, plus seizures >10 min						
Unique events						
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.....						

mITT = Intent-to-treat;

[1] Any AE with Status Epilepticus or presumed Epilepticus

[2] This includes all single seizures >10 minutes in duration as recorded in the subject's seizure diary. For each subject, the number of episodes is calculated; then the number per subject for each treatment group is obtained by summing across subjects in each group and dividing by number of subjects in that treatment group who had single seizures > 10 min.

Programming note: Use the same Table 14.2.9.1 shell for

Table 14.2.9.1.1
Number of episodes of status epilepticus (SE)
mITT Population (Japan)

Table 14.2.9.2
Duration of Seizures
mITT Population

Percentage of seizures by duration	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Baseline						
<2 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	NA
2-10 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	NA
>10 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	NA
OLE Treatment Period						
<2 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
2-10 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
>10 min	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX

mITT = modified Intent-to-treat; 95% CI are based on the exact (Clopper-Pearson) method. NA = Not Applicable.

Programming notes:

To calculate the probability of a seizure <2 min. for a given treatment group, for each subject, calculate the proportion of seizures < 2 min. For example, if the subject has a total of 5 seizures with 2 being <2 min in duration, their proportion is 2/5. Add these proportions for all subjects in the treatment group, and divide the total by the number of subjects to get the treatment group proportion of subjects with seizure duration <2 min. Then multiply the result by 100 to get the percentage.

Repeat for the other treatment groups. Repeat for seizure durations 2-10 min., and for >10 min.

Table 14.2.10.1
Clinical Global Impression of Improvement, Parent/Caregiver Rating
mITT Population

Categorical Description	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
OLE Month 1 (Visit 3)						
Summary Statistics						
n [1]	Xx	Xx	xx	Xx	xx	xx
Mean (SE)	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx
Number (%) of subjects responding at visit, by response category						
1=Very much improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2=Much improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3=Minimally improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4=No change	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5=Minimally worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6=Much worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7=Very much worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Much/very much Improved (1, 2): n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% CI*	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Minimally/much/very much Improved(1,2,3): n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% CI*	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Repeat for:						
OLE Month 2 (Visit 4)						
OLE Month 3 (Visit 5)						
OLE Month 6 (Visit 6)						
OLE Month 9 (Visit 7)						
OLE Month 12 (Visit 8)						
OLE Month 15 (Visit 9)						
OLE Month 18 (Visit 10)						

OLE Month 21 (Visit 11)						
OLE Month 24 (Visit 12)						
OLE Month 27 (Visit 13)						
OLE Month 30 (Visit 14)						
OLE Month 33 (Visit 15)						
OLE EOS/EOT (Visit 16)						
Summary Statistics						
n [1]	Xx	Xx	xx	Xx	xx	xx
Mean (SE)	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx	Xx, xx
Number (%) of subjects at visit, by response category						
1=Very much improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2=Much improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3=Minimally improved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4=No change	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5=Minimally worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6=Much worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7=Very much worse	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Much/very much improved (1, 2): n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% CI*	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Minimally/much/very much Improved(1,2,3): n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
95% CI*	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)

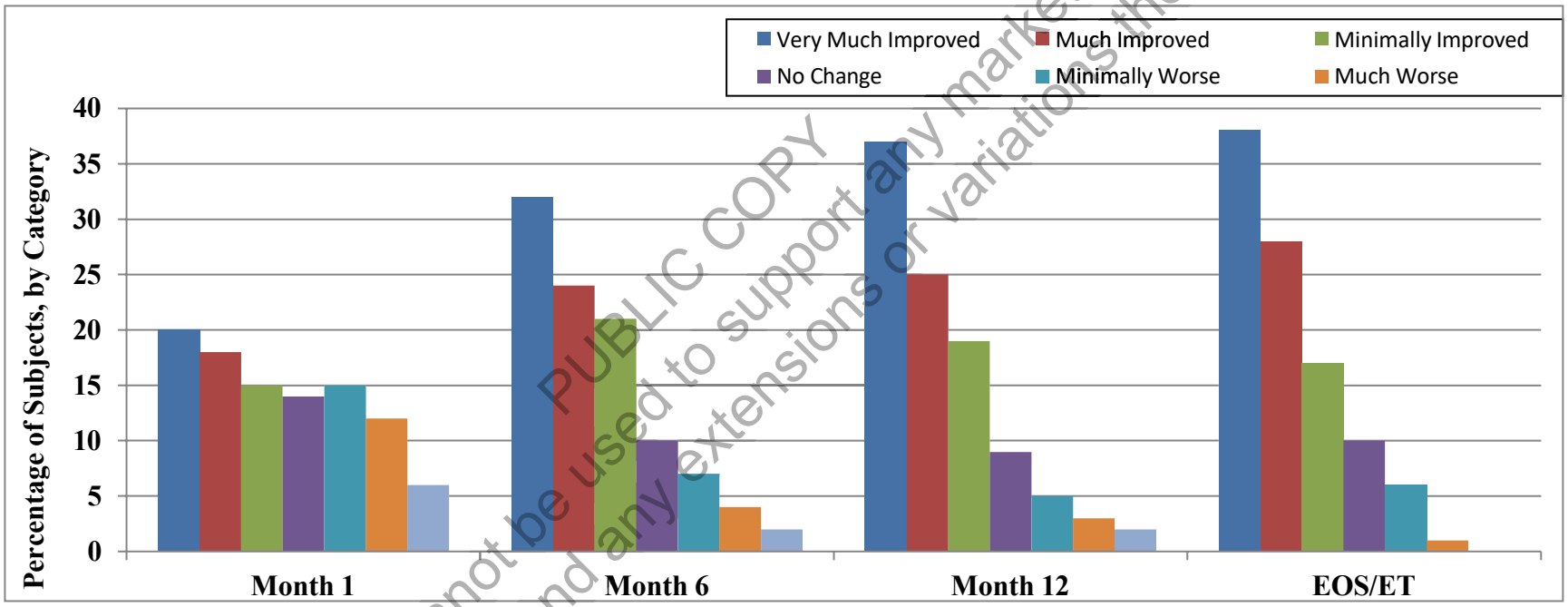
mITT = Modified Intent-to-treat; CI = Confidence Interval; SE = Standard Error; N= Number of subjects in population.
[1]n=number of subjects at time point; this is used as the denominator when calculating the percent of subjects responding in each CGI category and the percent who show improvement or much/very much improvement.
*Exact Clopper-Pearson two-sided confidence interval for the percentage of subjects with that response.

Programming note:
n – use the total for nonmissing responses
Here we are doing no comparisons, the 95% CI is for the percentage or proportion for that group (for interim, it's ZX008 OL) at that time point. Include all visits out through EOS visit.
Use the Table 14.2.10.1 shell for

Table 14.2.10.1.1
Clinical Global Impression of Improvement, Parent/Caregiver Rating
mITT Population (Japan)

Figure 14.2.10.2
Clinical Global Impression of Improvement, Parent/Caregiver Rating
mITT Population

Treatment Group=ZX008 0L



Programming Note:
Include all visits where the data is collected.
Use Labels
OLE Month 1 (Visit 3)
OLE Month 2 (Visit 4)
OLE Month 3 (Visit 5)

OLE Month 6 (Visit 6)
OLE Month 9 (Visit 7)
OLE Month 12 (Visit 8)
OLE Month 15 (Visit 9)
OLE Month 18 (Visit 10)
OLE Month 21 (Visit 11)
OLE Month 24 (Visit 12)
OLE Month 27 (Visit 13)
OLE Month 30 (Visit 14)
OLE Month 33 (Visit 15)
OLE EOS/EOT (Visit 16)
EOS/ET.

Note EOS/ET = Last Available Data Point during OLE. [For interim we are plotting for ZX008 OL.]
For interim analysis, only the ZX008 OL group (ie all subjects) is plotted.
Use the Figure 14.2.10.2 shell for

Figure 14.2.10.2.1
Clinical Global Impression of Improvement, Parent/Caregiver Rating
mITT Population (Japan)

Programming note: Use shell for Table 14.2.10.1 shell to produce the following.

Table 14.2.10.3
Clinical Global Impression of Improvement, Investigator Rating
mITT Population

Table 14.2.10.3.1
Clinical Global Impression of Improvement, Investigator Rating
mITT Population (Japan)

Programming note: Use shell for Figure 14.2..10.2 shell to produce the following.

Figure 14.2.10.4
Clinical Global Impression of Improvement, Investigator Rating
mITT Population

Figure 14.2.10.4.1
Clinical Global Impression of Improvement, Investigator Rating
mITT Population (Japan)

Table 14.2.11.1
Quality of Life in Childhood Epilepsy (QOLCE)
mITT Population

Domain	Subscale	Visit	Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XXX)	De Novo Subjects (N = XX)
Physical	Physical Restriction	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16)							

		EOS/EOT							
REPEAT FOR									
Physical	Physical Restrictions								
Physical	Energy/Fatigue								
Well-being	Depression								
Well-being	Anxiety								
Well-being	Control/helplessness								
Well-being	Self-esteem								
Cognition	Attention/Concentration								
Cognition	Memory								
Cognition	Language								
Cognition	Other Cognitive								
Social Activities	Social Interactions								
Social Activities	Social Activities								
Social Activities	Stigma Item								
Behavior	Behavior								
General Health	General Health Item								
Quality of Life	Quality of life Item								

Overall Quality of Life	Overall Quality of Life	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
			P-value*	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
		Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT							

mITT = Modified intent-to-treat; SD= Standard Deviation; N=Nmber of subjects with resposnes for that visit/time point.
*P-value is based on the Wilcoxon signed ranks test that the within-group change from baseline is different from 0.

Programming notes:
Note: For the interim, only the last column is analyzed and reported.
Note: For the final, to conserve space may use the domain and subscale as headers and start table using the Vist column
Note: Use question list for above tables as given below:

Domains and Subscales of QOLCE:

Domain	Subscale	Item
Section 3: Physical	Physical Restrictions	3.1 a-j
Section 3: Physical	Energy/Fatigue	3.2 a,b
Section 4: Well-being	Depression	4.1 a,d,e,l
Section 4: Well-being	Anxiety	4.1 b,g,j,n,o,p
Section 4: Well-being	Control/helplessness	4.1 c,f,h,i
Section 4: Well-being	Self-esteem	4.1 k,m,q,r,s
Section 5: Cognition	Attention/Concentration	5.1 a,d,e,f,g
Section 5: Cognition	Memory	5.1 j,k,l,m,n,o
Section 5: Cognition	Language	5.1 p,q,r,s,t,u,v,w
Section 5: Cognition	Other Cognitive	5.1 b,c,h
Section 6: Social Activities	Social Interactions	6.1 c,f,h
Section 6: Social Activities	Social Activities	6.1 a, e; 6.2
Section 6: Social Activities	Stigma Item	6.1 i
Section 7: Behavior	Behavior	7.1 a,c,f,g,h,i,j,k,l,m,o,q,r,s,t
Section 8: General Health	General Health	8.1
Section 2 (USA Version) or Section 9 (Australia Version)	Quality of lifeitem	2.1 or 9.1

For each treatment group at Baseline and End of Study/ET, the mean (SD) score will be presented for each QOLCE subscale and for the overall quality of life score. In addition, the change from baseline in the overall QOLCE will be calculated for each subject by subtracting the baseline overall score from the overall score measured at each visit. The change from baseline for each treatment group will be summarized by the mean (SD) and assiessed for significance using Wilcoxon signed-rank tests.

Revised 5/30/2017

Programming Note: see below for reverse coding and transformation of scores

To calculate subscale scores, the 5 point item scores will first be reverse coded as necessary so that scores of 5 represent the best possible response and 1 represents the worst possible response. Item scores will then be transformed to a 0-100 scale as follows: 1-0, 2-25, 3-50, 4-75, 5-100.

Item/Question No.	Reverse coded items*	Scale	Comments
3.1	c, d, e, f, g, h, I, j	1-5	
3.2	b	1-5	
4.1	b, d, f, k, l, m, q	1-5	
5.1	i	1-5	
6.1	b, d, g	1-5	
6.2		1-5	1=0; 2=25, 3=50, 4=75, 5=100
6.3**	6.3	1-5	Recode 1 to 4; 2 to 3; 3 to 2; 4 to 1. Do not recode "5"
6.4**	6.4	1-5	Recode 1 to 4; 2 to 3; 3 to 2; 4 to 1. Do not recode "5"
7.1	e, i, l, m, n, o, s, t,v	1-5	
8.1	8.1	1-5	
9.1	9.1	1-5	

Usual coding: 1=0, 2=25, 3=50, 4=75, 5=100.

*Reverse coded items.
For these, please code as follows: 1=100, 2=75, 3=50, 4=25, 5=0

**For 6.3 and 6.4, the (reverse coded)scores will be as follows:
1=75, 2=50 3=25, 4=0, 5=.

For 6.2, score as follows: 1=0, 2=25, 3=50, 4=75, 5=100.

Table 14.2.12.1
Pediatric Quality of Life Inventory (Peds QL)- (Version 4.0) – Parent Report
mITT Population

Functioning Area	Visit	Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XXX)	De Novo Subjects (N = XXX)
Physical	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value*	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16)							

	EOS/EOT							
REPEAT FOR								
Emotional								
Social								
School								
Physical Health Summary[1]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value*	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								

Psychosocial Health Summary[2]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value*	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Total Score[3]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX

		Mean (SD)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value*	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								

mITT = Modified intent-to-treat; SD = Standard Deviation; N=Number of subjects in population; n=number of subjects with responses for that visit/time point. EOS/ET=Last available measurement in OLE Treatment Period.

*Higher scores indicate better functioning

[1] The Physical Health Summary score is equal to the Physical Functioning Scale Score.

[2] Computed as the sum of the items over the number of items answered in the Emotional, Social, and School Functioning Scales.

[3]Computed as the sum of all the items over the number of items answered on all the Scales.

[4]P-value is based on the Wilcoxon signed ranks test that the within-group change from baseline is different from 0.

Programming note: Please see ZX008-1503 SAP section 6.3.3.7 for scoring instructions.

Table 14.2.12.2
PedsQL Family Impact Module (Version 2.0) – Parent Report
mITT Population

Functioning Area	Visit	Statistics	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Physical Functioning	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT							
REPEAT FOR								
Emotional Functioning								

Social Functioning								
Cognitive Functioning								
Communication								
Worry								
Daily Activities								
Family Relationships								
Parent HRQL[1]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value[4]	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Family Functioning[2]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX

		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value[4]	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx	x.xxxx
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Total Score[3]	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 (Visit 3)	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	OLE Month 1 Chg BL	n	XX	XX	XX	XX	XX	XX
		Mean (SE)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
		P-value[4]	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9)	n	XX	XX	XX	XX	XX	XX

	OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT							

mITT = Modified intent-to-treat; SD = Standard Deviation.
Notes:
EOS/ET=Last available measurement in OLE Treatment Period.
[1] Computed as the sum of the items divided by the number of items answered in the Physical, Emotional, Social, and Cognitive Functioning scales.
[2] Computed as the sum of the items divided by the number of items answered in the Daily Activities and Family Relationships scales.
[3] Computed as the sum of all 36 items divided by the number of items answered.
[4]P-value is based on the Wilcoxon signed ranks test that the within-group change from baseline is different from 0.

Programming note:
For each subject, be sure to calculate a scale score for each functioning area. Please see SAP for rules.
[1] Computed as the sum of the items divided by the number of items answered in the Physical, Emotional, Social, and Cognitive Functioning scales.
[2] Computed as the sum of the items divided by the number of items answered in the Daily Activities and Family Relationships scales.
[3] Computed as the sum of all 36 items divided by the number of items answered.
Please see SAP section 6.3.3.15 for full instructions.

Table 14.2.13.1
QOL of Parent/Caregiver Based on EQ-5D-5L – Health Profile Summary Original Response Categories
mITT Population

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Mobility	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Severe problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Extreme problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Self-care	Baseline	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Severe problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Extreme problem	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for								

OLE Month 2 (Visit 4)
OLE Month 3 (Visit 5)
OLE Month 6 (Visit 6)
OLE Month 9 (Visit 7)
OLE Month 12 (Visit 8)
OLE Month 15 (Visit 9)
OLE Month 18 (Visit 10)
OLE Month 21 (Visit 11)
OLE Month 24 (Visit 12)
OLE Month 27 (Visit 13)
OLE Month 30 (Visit 14)
OLE Month 33 (Visit 15)
OLE EOS/EOT (Visit 16)
EOS/EOT

Repeat summary for the domains:
Usual activities
Pain/discomfort
Anxiety/depression
Mobility
Self-care
Usual activities
Pain/discomfort

mITT = Modified Intent-to-treat;
Notes:
EOS/ET=Last available measurement in OLE Treatment Period.

Table 14.2.13.2:
QOL of Parent/Caregiver Based on EQ-5D-5L – Health Profile Summary Using Dichotomized Response Categories - mITT Population
mITT Population

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Mobility	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		No/slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate/severe/extreme problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Self-care	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		No/slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate/severe/extreme problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Usual activities	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		No/slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate/severe/extreme problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for								

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Pain/discomfort	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		No/slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate/severe/extreme problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11)				Continue for				

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								
Anxiety/depression	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX	XX
		No problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		No/slight problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Moderate/severe/extreme problems	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT								

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)

mITT = Modified Intent-to-treat;
Notes:
EOS/ET=Last available measurement in OLE Treatment Period.

Programming note: *This table repeats Table 14.2.13.1, with responses categorized into two levels.*

Table 14.2.13.3
QOL of Parent/Caregiver Based on EQ-5D-5L – Overall Health Status Using VAS (0-100) Scale
mITT Population

Overall Health Status	PBO-ZX008 OL (N = XX)		ZX 0.2 – ZX008 OL (N = XX)		ZX 0.5 – ZX008 OL (N = XX)		ZX 0.8 – ZX008 OL (N = XX)		ZX008 OL (N = XX)		De Novo Subjects (N = XX)	
Visit	Visit Value	Change from baseline	Visit Value	Change from baseline	Visit Value	Change from baseline	Visit Value	Change from baseline	Visit Value	Change from baseline	Visit Value	Change from baseline
OLE Baseline (Visit 1)												
n	Xx		Xx		Xx		Xx		Xx		Xx	
Mean	xx.x		xx.x		xx.x		xx.x		xx.x		xx.x	
SD	xx.xx		xx.xx		xx.xx		xx.xx		xx.xx		xx.xx	
Median	Xx.x		Xx.x		Xx.x		Xx.x		Xx.x		Xx.x	
Min	Xx		Xx		Xx		Xx		Xx		Xx	
Max	Xx		Xx		Xx		Xx		Xx		Xx	
OLE Month 1 (Visit 3)												
n	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Median	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x
Min	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
Max	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
P-value [1]		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx
…. Repeat for all visits												
OLE EOS/EOT (Month 36) Visit 16)												
n	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Median	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x
Min	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx

Max	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
P-value [1]		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx
EOS/EOT												
n	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Median	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x	Xx.x
Min	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
Max	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx	Xx
P-value [1]		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx		x.xxx

Notes:
EOS/ET=Last available measurement in OLE Treatment Period.
[1] P-value is based on the Wilcoxon signed ranks test that the within-group change from baseline is different from 0.

Table 14.2.14.1
QOL of Parent/Caregiver Based on Hospital Anxiety and Depression Scale (HADS): Normal, Borderline Abnormal and Abnormal Categories
mITT Population

Parameter	Visit	Category	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Anxiety	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX
		Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Borderline abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	End of study visit						
Depression	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX
		Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Borderline abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 8 (during Maintenance period)	…					
	End of study visit						
Total (Emotional Distress)	OLE Baseline (Visit 1)	n	XX	XX	XX	XX	XX
		Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Borderline abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	End of study visit						

mITT = Intent-to-treat; Note: This table includes those subjects from 1501 and 1502, and excludes subjects from 1504; the HADS was not assessed in subjects from 1504.

Table 14.2.14.2
QOL of Parent/Caregiver Based on Hospital Anxiety and Depression Scale (HADS): Summary Descriptive Statistics
mITT Population

Scale	Visit	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL(N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Anxiety	OLE Baseline (Visit 1)					
	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min	XX	XX	XX	XX	XX
	Max	XX	XX	XX	XX	XX
	End of study visit					
	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min	XX	XX	XX	XX	XX
	Max	XX	XX	XX	XX	XX
	Change from Baseline					
	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min	XX	XX	XX	XX	XX
	Max	XX	XX	XX	XX	XX
	95% CI	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)
	P-value[1]	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
Repeat for Depression and Total (Emotional Distress) Scores						

mITT = Intent-to-treat; SE = Standard Error. CI = Confidence Interval.
Note: The 95% confidence interval is based on the t-distribution.
[1] p-value from Wilcoxon signed-rank test.

Table 14.2.15.1
Study Medication Palatability Assessment
mITT Population

Visit	Response	PBO-ZX008 OL (N = XX)	ZX 0.2 – ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	ZX 0.8 – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
Item/Question							
OLE Month 1 (Visit 3)**		n=xxx	n=xxx	n=xxx	n=xxx	n=xxx	n=xxx
1. Medication Taste and Texture	Acceptable	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Not acceptable	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
2. Rating of Medication Taste	5 (likes very much)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	4 (likes it)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	3 (neutral)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	2 (dislikes)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	1 (dislikes very much)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing Response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	% liking it (4, 5)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	95% CI*	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
3. Problems administering medication due to taste or texture?	No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Every day	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Once or more every week	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Once or more during the month	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
OLE Month 2 (Visit 4)**		n=xxx	n=xxx	n=xxx	n=xxx	n=xxx	n=xxx
1. Medication Taste and Texture	Acceptable	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Not acceptable	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
2. Rating of Medication Taste	5 (likes very much)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)

	4 (likes it)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	3 (neutral)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	2 (dislikes)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	1 (dislikes very much)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing Response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	% liking it (4, 5)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	95% CI*	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
3. Problems administering medication due to taste or texture?	No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Every day	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Once or more every week	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Once or more during the month	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

mITT = modified Intent-to-treat.

*Exact Clopper-Pearson Confidence interval

** Study Medication Palatability Assessment was performed at Visits 3 and 4 only.

```
proc format;
   value likfmt  1='Very much improved'
              5=likes very much
              4=likes it
              3=neutral
              2=dislikes
              1=dislikes very much
              .=Missing Response;
 value likynfmt          0='No: Neutral or dislikes it'
                         1='Yes: Likes it ';
run;

data effdat;
 set alleff;
 if mittfl="Y";
```

```
 if anl01fl="Y";
 if aval ne .;
 likeityn=(aval ge 4.0);
run;
proc sort data=effdat out=effdat;
  by paramcd avisitn;

%macro exci_(type,param, paramfmt);
ods trace on;
ods output Binomial=bin_&type;
proc sort data=effdat; by paramcd avisitn descending &param;
proc freq data=effdat order=data;
  tables &param / out=outp&type exact binomial; **outp11 has percentages for table;
  by paramcd avisitn;
  format aval &param. &paramfmt.. ;
run;
data bin_&type;
  set bin_&type;
  if Name1 in ('XL_BIN', 'XU_BIN');
  cValue1=cValue1*100.0;  *****convert endpoint values from proportions to percentages;
  nValue1=nvalue1*100.0;
run;
%mend;

%exci_(lkt, likeityn, likynfmt);
```

Table 14.2.15.2
Sleep quality and mealtime behavior
mITT Population

Visit/Question	Response Category	PBO-ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	PK – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
OLE Baseline (Visit 1)		n=xxx	n=xxx	n=xxx	n=xxx	n=xxx
1. Child waking in night or very early in morning more than usual?	More disturbed than before	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Sleep pattern is same as before	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Sleeps better than before	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
2. Change in mealtime behavior since taking study medication?	Worsened mealtime behavior	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	No change in mealtime behavior	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Improved in mealtime behavior	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
	Missing Response	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)	XX (XX.XX%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT						

mITT = modified Intent-to-treat. Only subjects in feeder study 1504 were given this assessment. N=Total number of subjects in the population. n=number of subjects answering.
Notes:
EOS/ET=Last available measurement in OLE Treatment Period.

Table 14.2.15.3
Karolinska sleepiness scale: Frequency Distribution
mITT Population

	PBO-ZX008 OL (N = XX)	ZX 0.5 – ZX008 OL (N = XX)	PK – ZX008 OL (N = XX)	ZX008 OL (N = XX)	De Novo Subjects (N = XX)
OLE Baseline (Visit 1)	n=xxx	n=xxx	n=xxx	n=xxx	n=xxx
Score/Description					
1. Extremely alert	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2. Very alert	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3. Alert	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4. Rather alert	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
5. Neither alert nor sleepy	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
6. Some signs of sleepiness	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
7. Sleepy, but no effort to keep awake	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
8. Sleepy, some effort to keep awake	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
9. Very sleepy, great effort to keep awake, fighting sleep	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Active (1-6)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sleepy (7-9)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Continue for OLE Month 2 (Visit 4) OLE Month 3 (Visit 5) OLE Month 6 (Visit 6) OLE Month 9 (Visit 7) OLE Month 12 (Visit 8) OLE Month 15 (Visit 9) OLE Month 18 (Visit 10) OLE Month 21 (Visit 11) OLE Month 24 (Visit 12) OLE Month 27 (Visit 13) OLE Month 30 (Visit 14) OLE Month 33 (Visit 15) OLE EOS/EOT (Visit 16) EOS/EOT					

mITT = modified Intent-to-treat. Only subjects in feeder study 1504 were given this assessment. N=nmber of subjects eligible for assessment (subjects from 1504 who entered 1503). N=number answering at visit.
Notes:
EOS/ET=Last available measurement in OLE Treatment Period.

Table 14.3.1.1
Overview of number of subjects with TEAE during OLE Treatment Period
Safety Population

Number of Subjects with…	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=xx)	De Novo Subjects (N=xx)
Treatment-Emergent Adverse Events							
At least one TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least one Serious TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least one Fatal TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least one Related TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least one Related Serious TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least one TEAE Leading to Discontinuation of Study Treatment	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

TEAE = Treatment-Emergent Adverse Event.
Note: Percentages are calculated based on the number of subjects in the Safety population in each treatment group.
Note: Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.

Programming note: Use the Table 14.3.1.1 shell to produce

Table 14.3.1.1.1
Overview of number of subjects with TEAE during OLE Treatment Period
Safety Population (Japan)

Table 14.3.1.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class and Preferred Term	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	ZX008 OL (N=xx)	De Novo Subjects (N=xx)
Subjects with any TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.							

TEAE = Treatment-Emergent Adverse Event.
Note: Percentages are calculated based on the number of subjects in the Safety population.
Note: Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.
Note: A subject with more than one TEAE with the same preferred term is counted once for that term. A subject with more than one TEAE under a system organ class is counted once for that class.

Programming note: Use the Table 14.3.1.2.1 shell to produce same shell for 14.3.1.2.1.3 (Japan).

Table 14.3.1.2.1.3
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Table 14.3.1.2.1.1
Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (<6 yrs, ≥6 yrs), MedDRA System Organ Class and Preferred Term
Safety Population

Programming note: Similar to Table SADS21 in ISS, but population is 1503 Safety, and only use AEs occurring during 1503. One column only, ALL subjects in ZX008 OL. Alternatively, this is just the above Table, 14.3.1.2.1, by Age Group.

Programming Note: Use the shell for 14.3.1.2.1.1 to produce same format for 14.3.1.2.1.4.

Table 14.3.1.2.1.4
Treatment-Emergent Adverse Events during Open-label Treatment Periods by Age Group (< 6 yrs, ≥6 yrs), MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Table 14.3.1.2.1.2

Treatment-emergent Adverse Events with Decreased Appetite or Hypophagia during Open-Label Treatment Period
Safety Population

	Placebo (N = xxx)	ZX008 0.2 mg (N = XXX)	ZX008 0.5 mg (N = XXX)	ZX008 0.8 mg (N = XXX)	ZX008 OL (N = XXX)	De Novo Subjects (N = XXX)
Decreased Appetite	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Had adverse event unresolved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Duration of event for subjects who had event resolved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX	XX	XX	XX	XX	XX
Min, Max	XX	XX	XX	XX	XX	XX
Hypophagia	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Had adverse event unresolved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Duration of event for subjects who had event resolved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
n	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX	XX	XX	XX	XX	XX
Min, Max	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX

TEAE = Treatment-Emergent Adverse Event.

Note: Events considered are all TEAEs occurring during OLE. Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.

Programmin note: Please see annotations in ISS for SST16
Programming notes:If subjects has multiple events with the same preferred term, count the worst case (if one event is unresolved, count the unresolved one).
Programming Note: Use the same shell for 14.3.1.2.1.5 (Japan).

Programming Note: ***Use the shell for Table 14.3.1.2.1) for the following Tables:***

Table 14.3.1.2.2
Treatment-Emergent Adverse Events *occurring in at least 5% of the subjects by MedDRA System Organ Class and PT*
Safety Population

For the interim: Since we are only tabulating for "All subjects",
Add the footnote: "Events listed are those for which the % of subjects having that AE is ≥5.0% of subjects."

Table 14.3.1.3
TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term
Safety Population

Table 14.3.1.3.1
TEAEs leading to study discontinuation by MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Table 14.3.1.4
Serious TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

Table 14.3.1.4.1
Serious TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Table 14.3.1.5.1
Related TEAEs MedDRA System Organ Class and Preferred Term
Safety Population

Table 14.3.1.5.2
Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term
Safety population

Table 14.3.1.5.3
Related TEAEs MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Table 14.3.1.5.4
Related TEAEs occurring in at least 5% of subjects by MedDRA System Organ Class and Preferred Term
Safety population (Japan)

For the interim: Since we are only tabulating for “All subjects”,
Add the footnote: “Events listed are those for which the % of subjects having that AE is ≥5.0% of subjects.”

Table 14.3.1.6
TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class and Preferred Term	Maximum Severity	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	Gp 9 (N=xx)	De Novo Subjects (N=xx)
Subjects with any TEAE	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.....								
System Organ Class 2	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.....								

TEAE = Treatment-Emergent Adverse Event.
Note: Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.
Note: A subject with more than one TEAE with the same preferred term is counted once at the maximum severity for that term. A subject with more than one TEAE under a system organ class is counted once at the maximum severity for that class
Note: TEAEs with missing severity are considered severe in this summary

Programming Note: Use Table 14.3.1.6 shell for

Table 14.3.1.6.1
TEAEs by Maximum Severity, MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Programming Note: use shell from Table 14.3.1.1 to produce the following tables.

Table 14.3.1.7
Overview of number of subjects with Treatment-Emergent Adverse Events of Special Interest
Safety Population

Table 14.3.1.7.1
Overview of number of subjects with Treatment-Emergent Adverse Events of Special Interest
Safety Population (Japan)

Add footnote: AESI=Adverse event of sepcial interest.

Programming Note: use shell from Table 14.3.1.2.1 for

Table 14.3.1.8
Treatment Emergent Adverse events of special interest (TE AESI) by MedDRA System Organ Class and Preferred Term
Safety Population

Table 14.3.1.8.1
Treatment Emergent Adverse events of special interest (TE AESI) by MedDRA System Organ Class and Preferred Term
Safety Population (Japan)

Please change footnote from TEAE to TE AESI=Treatment emergent adverse event of special interest.

Table 14.3.1.9.1
Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population

MedDRA System Organ Class and Preferred Term	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	Gp 9 (N=xx)
Subjects with Any Non-TEAE Starting Between Visits 12 and 13 of Feeder Study	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
.						
.						

TEAE = Treatment-Emergent Adverse Event.
Note: Percentages are calculated based on the number of subjects in the Safety population.
Note: Adverse events in this table have a start date preceding the start of treatment in Study 1503, hence were classified as "non-treatment-emergent".
Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.
Note: A subject with more than one non-TEAE with the same preferred term is counted once for that term. A subject with more than one Non-TEAE under a system organ class is counted once for that class.

Programming Note: Include only events whose start date is between Day -30 (inclusive) and Day -1 (inclusive), counting study days from beginning of OLE Treatment period, not core. There will be no De Novo Column for this table.

Use the Table 14.3.1.9.1 shell for

Table 14.3.1.9.1.1
Non-treatment Emergent Adverse Events Starting between Visits 12 and 13 of the Feeder Study, by MedDRA System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population (Japan)

Table 14.3.1.9.2
TEAEs starting in the 1st month of OLE by System Organ Class, Preferred, Term and Prior Treatment in Feeder Study
Safety Population

MedDRA System Organ Class and Preferred Term	Gp1 (N=xx)	Gp 2 (N=xx)	Gp3 (N=xx)	Gp 4 (N=xx)	Gp5 (N=xx)	De Novo Subjects (N=xx)
Subjects with any TEAE starting in the first month.	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

TEAE = Treatment-Emergent Adverse Event.

Note: A subject with more than one TEAE with the same preferred term is counted once for that term. A subject with more than one TEAE under a system organ class is counted once for that class.

Programming note:
Include only events starting on or after Day 1 up to Day 30 (counting from beginning of OLE Treatment period, NOT Core).
Use same Table 14.3.1.9.2 shell for

Table 14.3.1.9.2.1
TEAEs starting in the 1st month of OLE by System Organ Class, Preferred, Term and Prior Treatment in Feeder Study
Safety Population (Japan)

Programing note: Use the 14.3.1.9.1 shell to produce the following tables. Include only events starting on or after Study Day31 up to Day 60 (counting from beginning of OLE Treatment period, NOT Core)

Table 14.3.1.9.3
TEAEs starting in the 2nd month of OLE by System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population

Table 14.3.1.9.3.1
TEAEs starting in the 2nd month of OLE by System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population (Japan)

Programing note: Use the Table 14.3.1.9.1 shell for the following tables. Include only events starting on or after Study Day61 up to day 90(counting from beginning of OLE Treatment period, NOT Core)

Table 14.3.1.9.4
TEAEs starting in the 3rd month of OLE by System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population

Table 14.3.1.9.4 .1
TEAEs starting in the 3rd month of OLE by System Organ Class, Preferred Term and Prior Treatment in Feeder Study
Safety Population (Japan)

Table 14.3.1.10.1
Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days)
Safety Population

MedDRA System Organ Class and Preferred Term	Placebo (N=xx) n (%)/ Mean Onset/ Mean Duration	ZX008 0.2 mg/kg/day (N=xx) n (%)/ Mean Onset/ Mean Duration	ZX008 0.5 mg/kg/day (N=xx) n (%)/ Mean Onset/ Mean Duration	ZX008 0.8 mg/kg/day (N=xx) n (%)/ Mean Onset/ Mean Duration	Any DB ZX008 (N=xx) n(%) Mean Onset/ Mean Duration
Subjects with any TEAE starting in the first month.	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
System Organ Class 1	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
Preferred Term 1	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
Preferred Term 2	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x

TEAE = Treatment-Emergent Adverse Event.
TEAE = Treatment-Emergent Adverse Event.
Note: Percentages are calculated based on the number of subjects in each treatment group.
Note: Mean Onset and Mean Duration are measured in days. The onset day is the study day at the adverse event onset. The duration is the number of days from onset to resolution or from onset to last follow-up day if the event was ongoing.
Note: Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.
Note: In subjects with more than one occurrence of the same event, the time to onset and duration is based on the earliest occurring event.
Note: Time to onset is the number of days since first treatment with either ZX008 or placebo. The duration of an event is limited to the period of the double-blind study.
Note: A subject with more than one TEAE with the same preferred term is counted once for that term. A subject with more than one TEAE under a system organ class is counted once for that class.

Programing note: Use shell for 14.3.1.10.1 for 14.3.1.10.1.1

Table 14.3.1.10.1.1
Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind Treatment Period by MedDRA System Organ Class and Preferred Term with Mean Time to Onset (days) and Mean Duration (days)
Safety Population (Japan)

Table 14.3.1.10.2
Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days)
Safety Population

MedDRA System Organ Class and Preferred Term	ZX008 0 - < 0.2 mg/kg [1] (N=xx) n (%)/ Mean Onset/ Mean Duration	ZX008 0.2 - < 0.4 mg/kg (N=xx) n (%)/ Mean Onset/ Mean Duration	ZX008 0.4 - < 0.6 mg/kg n (%)/ Mean Onset/ Mean Duration	ZX008 0.6 - < 0.8 mg/kg (N=xx) n (%)/ Mean Onset/ Mean Duration	Any OLE ZX008 (N=xx) n(%) Mean Onset/ Mean Duration
Subjects with any TEAE starting in the first month.	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
System Organ Class 1	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
Preferred Term 1	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
Preferred Term 2	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x	XX (XX.X%) / xx.x /xx.x
.					
.					

TEAE = Treatment-Emergent Adverse Event.
Note: Percentages are calculated based on the number of subjects in each treatment group.
Note: Mean Onset and Mean Duration are measured in days. The onset day is the study day at the adverse event onset. The duration is the number of days from onset to resolution or from onset to last follow-up day if the event was ongoing.
Note: Adverse events are classified as treatment-emergent if they started on or after the date of first dose of study treatment. Adverse events with partial or missing start dates are classified as treatment-emergent, unless the non-missing components of the start date confirm otherwise.
Note: In subjects with more than one occurrence of the same event, the time to onset and duration is based on the earliest occurring event.
Note: Onset day is measured from the first date of ZX008 treatment to onset. Duration for the TEAEs in the placebo group start after the subject starts ZX008 treatment in the OLE.
[1] For subjects treated with Placebo in the core study, TEAEs are counted only after the subject started ZX008 treatment.

Programming note: Use the shell for Table 14.3.1.10.2.1.

Table 14.3.1.10.2.1
Treatment-Emergent Adverse Events that Occurred in at least 5% of Subjects during Double-blind through Open-label Treatment Periods by MedDRA System Organ Class and Preferred Term, Mean Average Dose in ZX008-1503 with Mean Time to Onset (days) and Mean Duration (days)
Safety Population (Japan)

Programming Notes: Use the Listing 16.2.7.1 shell for the following tables.

Table 14.3.2.1
Listing of Deaths

Table 14.3.2.1.1
Listing of Deaths (Japan)

Table 14.3.2.2
Listing of SAEs

Table 14.3.2.2.1
Listing of SAEs (Japan)

Table 14.3.2.3
Listing of Discontinuations Due to AE

Table 14.3.2.3.1
Listing of Discontinuations Due to AE (Japan)

Laboratory Data

Please see below (also in SAP) for time windows

Time Intervals for Analysis Visits for Laboratory Data and Vital Signs

Analysis Phase/Period	Scheduled Visit Number **in ZX008-1503**	Analysis Visit Number*	Time Interval (label on output)	Time Interval (Day)	Target Time Point (Day)
Pre-OLE	1	1	Baseline (OLE)	1	1
OLE	2	2	Week 2 (OLE)	2 to 20	15
OLE	3	3	Month 1 (OLE)	21 to 44	30
OLE	4	4	Month 2 (OLE)	45 to 74	60
OLE	5	5	Month 3 (OLE)	75 to 134	90
OLE	6	6	Month 6 (OLE)	135 to 224	180
OLE	7	7	Month 9 (OLE)	225 to 314	270
OLE	8	8	Month 12 (OLE)	315 to 409	365
OLE	9	9	Month 15 (OLE)	410 to 499	455
OLE	10	10	Month 18 (OLE)	500 to 589	545
OLE	11	11	Month 21 (OLE)	590 to 679	635
OLE	12	12	Month 24 (OLE)	680 to 774	730
OLE	13	13	Month 27 (OLE)	775 to 864	820
OLE	14	14	Month 30 (OLE)	865 to 954	910
OLE	15	15	Month 33 (OLE)	955 to 1044	1000
OLE	16	16	Month 36 (OLE)	1045 to 1109	1095
OLE	OLE last Visit**	99	Last Value	Day 2 to Visit 17 date	

Programming Notes:
*For multiple measurements within a time window, please use the closest to the target time point. Note that measurements occurring on the end date of a phase/period or start date of a new phase/period are assigned to the preceding phase/period. For example, measurements taken on OLE Study Day1 are assigned as Baseline (OLE).
**The last observation in the time window will be used. *[This is an exception from the rule in the preceding note.]*

Table 14.3.4.1
Laboratory parameters – Hematology
Safety Population

Laboratory Test: *Parameter* (units)

	ZX008 OL (N=xxx)		De Novo Subjects (N=xxx)	
Visit	Visit Values	Change from Baseline	Visit Values	Change from Baseline
Baseline (OLE)				
N	XX		XX	
Mean	XX.X		XX.X	
SD	XX.XX		XX.XX	
Median	XX.X		XX.X	
Min	XX		XX	
Max	XX		XX	
Week 2 (OLE)				
N	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX
Max	XX	XX	XX	XX
Repeat for other time periods: Month 2 (OLE), 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, and Last Value (OLE)				

Table 14.3.4.1
Laboratory parameters – Hematology
Safety Population

Laboratory Test: *Parameter* (units)

Visit [1]	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	Gp5 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N =XX)
Baseline (OLE)							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX	XX
Week 2 (OLE)							
Observed							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX	XX
CFB							
N	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX	XX
…							
Repeat for all time points							

CFB = Change from Baseline.
Note: Time windows are specified in the Statistical Analysis Plan. For multiple measurements within a time window, the closest to the target time point was used. Measurements occurring on the end date of an interval or start date of a new interval are assigned to the preceding interval: For example, measurements taken on OLE Study Day1 are assigned as Baseline(OLE). However, for the Last value (OLE) , the last observation in the time window is used.
[1] Laboratory tests were performed at all visits

Programming Note:

- ***Repeat for all other laboratory parameters.***
- ***Use correct number of decimal places for summary statistics depending on the raw data recorded for each parameter.*** Please do not use more than 3 decimal places unless there are 2 significant digits or fewer. Two decimal places are preferred.
- ***Include correct units for the lab tests in the titles.***

Programming Notes: ***Use the table shell for 14.3.4.1 for the following tables.***

Table 14.3.4.1.1
Laboratory parameters – Hematology
Safety Population (Japan)

Table 14.3.4.2 Laboratory parameters –Biochemistry
Safety Population

Table 14.3.4.2.1 – Laboratory parameters – Biochemistry
Safety Population (Japan)

Table 14.3.4.4.1
Laboratory Parameters - Urinalysis (Quantitative Parameters)
Safety Population

Table 14.3.4.4.1.1
Urinalysis (Quantitative Parameters)
Safety Population (Japan)

Table 14.3.4.4.2
Laboratory parameters - Urinalysis (Categorical)
Safety Population

Laboratory Test: *Parameter [Example Table below for illustrative purpose only]*
Programming Note: For interims and 120-day, please use only last column ZX008 OL

	Gp1 (N=39)	Gp2 (N=40)	Gp3 (N=5)	Gp4 (N=43)	Gp5 (N=14)	Gp9 (N=141)	De Novo Subjects((N=XXX)
Baseline (OLE)							
n	34	36	3	38	0	111	111
NEGATIVE	34 (100.0%)	36 (100.0%)	3 (100.0%)	38 (100.0%)	0 (0.0%)	111 (100.0%)	111 (100.0%)
Week 2 (OLE)							
n	2	2	0	1	0	5	5
NEGATIVE	2 (100.0%)	2 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	5 (100.0%)	5 (100.0%)
Month 1 (OLE)							
n	29	31	2	34	10	106	106
NEGATIVE	29 (100.0%)	31 (100.0%)	2 (100.0%)	34 (100.0%)	10 (100.0%)	106 (100.0%)	106 (100.0%)
Month 2 (OLE)							
n	26	30	2	33	10	101	101
NEGATIVE	26 (100.0%)	30 (100.0%)	2 (100.0%)	33 (100.0%)	10 (100.0%)	101 (100.0%)	101 (100.0%)
.....							
Repeat for all visits							
Last Value (OLE)							
n	26	30	2	33	10	101	101
NEGATIVE	26 (100.0%)	30 (100.0%)	2 (100.0%)	33 (100.0%)	10 (100.0%)	101 (100.0%)	101 (100.0%)

Note: Time windows are specified in the Statistical Analysis Plan. For multiple measurements within a time window, the closest to the target time point was used. Measurements occurring on the end date of an interval or start date of a new interval are assigned to the preceding interval: For example, measurements taken on OLE Study Day1 are assigned as Baseline(OLE). However, for the Last value (OLE) , the last observation in the time window is used.

Programming Note: Use the Table 14.3.4.4.2 shell to produce the following table.

Table 14.3.4.4.2.1
Laboratory parameters - Urinalysis (Categorical)
Safety Population (Japan)

Table 14.3.4.5.1
Laboratory parameters – Tests of growth, precocious puberty and thyroid function
Safety Population (Japan)

Programming Note: Use Table 14.3.4.1 shell for the following tables.

Table 14.3.4.5
Laboratory parameters – Tests of growth, precocious puberty and thyroid function
Safety Population

Table 14.3.4.5.1
Laboratory parameters – Tests of growth, precocious puberty and thyroid function
Safety Population (Japan)

For interims and 120-day, please use only last column
For IDMC uses all columns

Programming Note: Use shell for Table 14.3.4.1 Include correct units in the titles for the Vital sign parameter

Table 14.4.1.1
Vital Signs
Safety Population

Table 14.4.1.1.1
Vital Signs
Safety Population (Japan)

Programming Note:

Use shell for Figure 1b in ISS for the the following figures.

Figure 14.4.1.2
Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period
Safety Population

Figure 14.4.1.2.1
Scatterplot of Age (X-axis) and Height (Y-axis) at End of Study during the Open-label Treatment Period
Safety Population (Japan)

Y-axis: ADVS.AVAL where PARAMCD=HEIGHT and AVISIT=EOS/ET and SAFFL='Y'
X-axis: ADSL.AGEEOS

Table 14.4.1.3

Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics
Safety Population

Age Group: 2-<4 years/ 4 -<6 years/ 6 - <12 years/>=12 years

Visit [1]	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	Gp5 (N = XX)	Gp9 (N = XX)
Baseline (OLE)						
N	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
Week 2 (OLE)						
Observed						
N	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
CFB						
N	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min	XX	XX	XX	XX	XX	XX
Max	XX	XX	XX	XX	XX	XX
...						

Repeat for all time points						

Note: If a test is repeated at any given visit, the last non-missing result is used in the summary.
Note: this table excludes the De Novo Subjects.

Programming note: Use the Table 14.4.1.3 shell for

Table 14.4.1.3.1
Weight during the Open-Label Study Period over Time by Age Group (2 - <4; 4 - <6; 6 to <12; and ≥12): Summary Statistics
Safety Population (Japan)

Table 14.4.1.4

Weight Over Time during the Open-Label Study Period for De Novo Subjects: Summary Statistics
Safety Population – De Novo Subjects

Visit [1]	De Novo Subjects (N = XX)
Baseline (OLE)	
N	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
Min	XX
Max	XX
Week 2 (OLE)	
Observed	
N	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
Min	XX
Max	XX
CFB	
N	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
Min	XX
Max	XX
…	
Repeat for all time points	

Note: If a test is repeated at any given visit, the last non-missing result is used in the summary.

Programming note: Use the Table 14.4.1.4 shell for

Table 14.4.1.4.1

Weight Over Time during the Open-Label Study Period for De Novo Subjects: Summary Statistics

Safety Population – De Novo Subjects – Japan

Table 14.4.1.5
Weight Summary (Lost/Gain ≥7% or ≥10%) during the Open-Label Study Period
Safety Population

	Placebo/ ZX 008 OL (N = XX)	ZX008 0.2 mg/ ZX 008 OL (N = XX)	ZX008 0.5 mg/ ZX008 OL (N = XX)	ZX008 0.8 mg/ ZX 008 OL (N = XX)	All Subjects (N = XX)	De Novo Subjects (N = XX)
Baseline (OLE) n	xx	xx	xx	xx	xx	xx
At Any Visit in OLE, n	xx	xx	xx	xx	xx	xx
Lost >=7% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Recovered lost weight [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Days until Recovery						
Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
SD	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Min	XXX	XXX	XXX	XXX	XXX	XXX
Max	XXX	XXX	XXX	XXX	XXX	XXX
Lost >=10% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gain >=7% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gain >=10% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Month 1 (OLE), n	xx	xx	xx	xx	xx	xx
Lost >=7% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Recovered lost weight [2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Days until Recovery						
Mean	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
SD	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
Median	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Min	XXX	XXX	XXX	XXX	XXX	XXX
Max	XXX	XXX	XXX	XXX	XXX	XXX
Lost >=10% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gain >=7% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Gain >=10% of weight [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Note: Time windows are specified in the statistical analysis plan. In the event of 2 or more assessments in the interval, the assessment completed closest to the target time point are assessed. For the last assessment, the last non-missing value observed.
[1] Percentages are based on the number of subjects with a baseline weight and a weight at the visit meeting the criteria noted in the row.
[2] A subject recovered, if they had a weight recorded after the visit being summarized that was within 1% of the baseline body weight at 2 consecutive visits. Percentages are based on the number of subjects who had the 7%/10% weight loss and had a value meeting the criteria noted in the row.

Programming Notes: Use the Table 14.4.1.5 shell for the following tables.

Table 14.4.1.5.1
Weight Summary (Lost/Gain ≥7% or ≥10%) during the Open-Label Study Period
Safety Population (Japan)

Table 14.4.1.6
Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate
Safety Population

Table 14.4.1.6.1
Weight Summary (Lost/Gain ≥7%, or ≥10%) during the Open-Label Study Period by Concomitant Topiramate
Safety Population (Japan)

Programming notes: Repeat Table 14.4.1.5 for 14.4.1.6 and 14.4.1.6.1 by subset by (a) subjects on concomitant topiramate, and (b) subjects not on concomitant topiramate.

Programming note: Use the Table 14.4.1.5 shell but only present for 5% to produce the following tables.

Table 14.4.1.7
Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period
Safety Population

Table 14.4.1.7.1
Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period
Safety Population (Japan)

Table 14.4.1.8
Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period by Concomitant Topiramate
Safety Population

Table 14.4.1.8.1
Weight Summary (Lost/Gain ≥5%) during the Open-Label Study Period by Concomitant Topiramate
Safety Population (Japan)

Table 14.4.4.1
Tanner Staging by Age Group for Boys
Safety Population

Age Group	Visit [1]	Tanner Stage	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	Gp5 (N = XX)	Gp9 (N = XX)
<7years	Baseline (OLE)(Day 1)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 6 (Month 6)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 12 (Month 24)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Final Visit/EOS	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>7years to <=11	Baseline (OLE)(Day1)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 6 (Month 6)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 12 (MNonth 24)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Final Visit/EOS	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>11years to <=15	Baseline (OLE) (Day 1)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 6 (Month 6)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

	Visit 12	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Final Visit/EOS	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>15years to <=18	Baseline (OLE) (Day 1)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 6 (Month 6)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Visit 12 (Month 24)	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Final Visit/EOS	Stage I	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage II	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage III	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
		Stage IV	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Stage V	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

[1] Per protocol amendment 3.0, Tanner Staging was to be completed at Baseline (Visit 1), and Months 6, 15, 27 and 36.

Programming Note: use shell from Table 14.4.4.1 for

Table 14.4.4.1.1
Tanner Staging by Age Group for Boys
Safety Population (Japan)

Table 14.4.4.1.2
Tanner Staging by Age Group for Girls
Safety Population

Table 14.4.4.1.2.1
Tanner Staging by Age Group for Girls
Safety Population (Japan)

Table 14.4.5.1
Number of Subjects with Suicidal Ideation, Suicidal Behavior and Self Injurious Behavior Without Suicidal Intent
Based on the (C-SSRS) during Treatment
Safety Population

Period	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	Gp5 (N = XX)	Gp9 (N = XX)	De Novo Subjects (N = XX)
Baseline (Visit 1 of OLE) [1]							
No.of Subjects Completing CSSRS							
No.of Subjects with Any Suicidal Ideation							
No.of Subjects with Any Suicidal Behavior							
No.of Subjects without Suicidal Ideation or Suicidal Behavior							
No. of Subjects with 'Self-injurious behavior without suicidal intent'							
OLE Period [2]							
No.of Subjects Completing CSSRS							
No.of Subjects with Any Suicidal Ideation							
No.of Subjects with Any Suicidal Behavior							
No.of Subjects without Suicidal Ideation or Suicidal Behavior							
No. of Subjects with 'Self-injurious behavior without suicidal intent'							

C-SSRS: Columbia Suicide Severity-Rating Scale

[1] Counts are based on response at Visit 1 of the OLE Period.

[2] Counts are based on responses during the OLE period.

Note: each subject is counted only once, using the most severe C-SSRS response category during treatment. No event=0; suicidal ideation=1, 2, 3, 4, 5; suicidal behavior=6, 7, 8, 9, 10. See SAP Section 6.4.10.
N=number of subjects with baseline AND post-baseline C-SSRS assessment. Cell frequencies are to be divided by the total N in the relevant treatment group and multiplied by 100 to get the cell %.

Programming note: Use the Table 14.4.5.1 shell for:

Table 14.4.5.1.1
Number of Subjects with Suicidal Ideation, Suicidal Behavior and Self Injurious Behavior Without Suicidal Intent
Based on the (C-SSRS) during Treatment
Safety Population (Japan)

Table 14.4.5.2
Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the (C-SSRS) during Treatment
Safety Population

	-----**Most Severe Post Baseline Potentially Suicide-Related Category**----			
BASELINE (OLE)	No suicidal ideation or behavior	Suicidal ideation	Suicidal behavior	Total
Gp1 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gp2 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gp3 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gp4 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gp5 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Gp9 (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
De Novo Subjects (N=xxx)				
No suicidal ideation or behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal ideation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Suicidal behavior	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

C-SSRS: Columbia Suicide Severity-Rating Scale

Programming Notes: Use the 14.4.5.2.shell for

Table 14.4.5.2.1
Number of Subjects with Suicide-Related Treatment-Emergent Events Based on the (C-SSRS) during Treatment
Safety Population (Japan)

Table 14.4.6.1
Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table
Safety Population

Scale/Index	Visit	Statistics	Gp1 (N = XX)	Gp2 (N = XX)	Gp3 (N = XX)	Gp4 (N = XX)	Gp5 (N = XX)	Gp9 (N = XX)
SCALES								
Inhibit	OLE Baseline	n						
		Mean (SE)						
	OLE Month 1	n						
		Mean (SE)						
	OLE Month 1 Chg BL	n						
		Mean (SE)						
	OLE Month 2	n						
		Mean (SE)						
	OLE Month 2 Chg BL	n						
		Mean (SE)						
	OLE Month 3	n						
		Mean (SE)						
	OLE Month 3 Chg BL	n						
		Mean (SE)						
	OLE Month 6	n						

		Mean (SE)						
	OLE Month 6 Chg BL	n						
		Mean (SE)						
	OLE Month 9	n						
		Mean (SE)						
	OLE Month 9 Chg BL	n						
		Mean (SE)						
	OLE Month12	n						
		Mean (SE)						
	OLE Month 12 Chg BL	n						
		Mean (SE)						
	… Repeat for OLE Months 15, 18, 21, 24, 27, 30, 33, 36							
	OLE Last Visit	n						
		Mean (SE)						
	OLE Last Visit Chg BL	n						
		Mean (SE)						
….								
[REPEAT for								
Shift								

Emotional Control (EC)								
Working Memory (WM)								
Plan/Organize (PO)]								
INDEXES								
Inhibitory Self-Control Index (ISCI) (Inhibit + EC)[1]	OLE Baseline	n						
		Mean (SE)						
	OLE Month 1	n						
		Mean (SE)						
	OLE Month 1 Chg BL	n						
		Mean (SE)						
	OLE Month 2	n						
		Mean (SE)						
	OLE Month 2 Chg BL	n						
		Mean (SE)						
	OLE Month 3	n						
		Mean (SE)						
	OLE Month 3 Chg BL	n						
		Mean (SE)						

	OLE Month 6	n						
		Mean (SE)						
	OLE Month 6 Chg BL	n						
		Mean (SE)						
	OLE Month 9	n						
		Mean (SE)						
	OLE Month 9 Chg BL	n						
		Mean (SE)						
	OLE Month12	n						
		Mean (SE)						
	OLE Month 12 Chg BL	n						
		Mean (SE)						
	… Repeat for OLE Months 15, 18, 21, 24, 27, 30, 33, 36							
	OLE Last Visit	n						
		Mean (SE)						
	OLE Last VisitChg BL	n						
		Mean (SE)						

		90% CI for change from BL[5]	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)	(xxx.x, xxx.x)
.....								
REPEAT FOR								
Flexibility Index (FI) (Shift + EC)[2]								
Emergent Metacognition Index (EMI) (WM + PO)[3]								
Global Executive Composite (GEC) (Inhibit + Shift + EC + WM + PO) [4]								

The BRIEF-P questionnaire was administered to preschool age children. N=# subjects in analysis population; n=number of subjects assessed at time point.
mITT = Modified Intent-to-Treat; SE=Standard Error; Chg. BL=Change from Baseline; EOS/ET=End-of-Study/Early Termination or Last available measurement.
Notes:
[1] ISCI: Computed as the sum of the scale raw scores obtained for Inhibit and Emotional Control.
[2] FI: Computed as the sum of the raw scale scores obtained for Shift and Emotional Control
[3] EMI: Computed as the sum of the raw scale scores for Working Memory and Plan/Organize.
[4] GEC: Inhibit + Shift + EC + WM + PO
[5] Based on T distribution. Endpoints of the interval are Mean ± T*SE, where T is obtained as the 95% percentile from the Student's T distribution with n-1 degrees of freedom

Programming notes:

1. The rater's responses are scored as follows: 1=Never, 2=Sometimes, and 3=Often

Scales of the BRIEF-P

Scale	No. of items	Items	Scoring Instructions (for each individual)*
Inhibit	16	3, 8, 13, 18, 23, 28, 33, 38, 43, 48, 52, 54, 56, 58, 60, 62	Add up scores for items on the scale
Shift	10	5, 10, 15, 20, 25, 30, 35, 40, 45, 50	Add up scores for items on the scale
Emotional Control	10	1, 6, 11, 16, 21, 26, 31, 36, 41, 46	Add up scores for items on the scale
Working Memory	17	2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 51, 53, 55, 57, 59, 61, 63	Add up scores for items on the scale
Plan/Organize	10	4, 9, 14, 19, 24, 29, 34, 39, 44, 49	Add up scores for items on the scale
Validity scales			
Inconsistency	10 pairs	(1, 11), (3, 33), (5, 45), (10, 20), (11, 26), (16, 21), (18, 52), (33, 38), (43, 52), (48, 54)	For each item in a pair, obtain the score for each item, and subtract the scores, keeping the absolute difference. Sum the 10 absolute differences to get the Inconsistency score. Classification[1]: 0-6: Acceptable 7 Acceptable ≥8: Inconsistent
Negativity	10	30, 44, 46, 47, 53, 55, 56, 57, 59, 63	Count the number of items with a score of 3. That is the negativity score. Classification[1]: 0-2 Acceptable 3 Acceptable ≥4 Elevated

2. *Missing data handling for the BRIEF-P[2]

1. First obtain the number of missing responses for the entire questionnaire of 63 items.

2. If the total number of unanswered items is >12, do not compute any of the (five) scale raw scores (I, S, EC, WM, PO) for the BRIEF-P, as per the authors, the "protocol should be considered invalid". In that case, all the scale raw scores will be missing, and the index scores will be missing as well.

3. If more than 2 (of the 63) items on the BRIEF-P have missing responses for a Scale (any of the 5 listed above), then a scale raw score should not be calculated. However, for any scale with 2 or fewer missing responses, impute a score of "1" for the missing item

References:

[1] Gioia GA, Espy KA, Isquith PK. BRIEF-P: Behavior Rating Inventory of Executive Function-Preschool Version. Professional Manual. 2003 Edition. Pages 15-16.

[2] Gioia GA, Espy KA, Isquith PK. BRIEF-P: Behavior Rating Inventory of Executive Function-Preschool Version. Professional Manual. 2003 Edition. Page 7."Missing Responses".

Programming Notes: Use the sheel for 14.4.6.1 for the following tables.

Table 14.4.6.1.1
Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) – Scoring summary table
Safety Population (Japan)

Table 14.4.6.2
Behavior Rating Inventory of Executive Function- (BRIEF)
Safety Population

Table 14.4.6.2.1
Behavior Rating Inventory of Executive Function- (BRIEF)
Safety Population (Japan)

For 14.4.6.2 and 14.4.6.2.1,
Scales are:

Inhibit
Shift
Emotional Control (EC)
Initiate
Working Memory (WM)
Plan/Organize (PO)
Organization of Materials (OM)
Monitor

For Indexes Part, where we use the 90% CI for the EOS/ET measurement, the following are used, along with relevant footnotes;

Behavioral Regulation Index (BRI)[1]
Metacognition Index (MI)[2]
Global Executive Composite (GEC) [3]

For the following line, include [4] as footnote
90% CI for change from BL[4]

Footnotes

The BRIEF questionnaire was administered to school age children. N=# subjects in analysis population; n=number of subjects assessed at time point.
mITT = Modified Intent-to-Treat; SE=Standard Error; Chg. BL=Change from Baseline; EOS/ET=End-of-Study/Early Termination or Last available measurement
Notes:
[1] Computed as the sum of the scale raw scores obtained for Inhibit, Shift, and Emotional Control.
[2] Computed as the sum of the raw scale scores obtained for Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor.
[3]Computed as the sum of the raw scale scores for BRI and MI.
[4]Based on T distribution. Endpoints of the interval are Mean ± T*SE, where T is obtained as the 95% percentile from the Student's T distribution with n-1 degrees of freedom

Programming notes:

1. The rater's responses are scored as follows: 1=Never, 2=Sometimes, and 3=Often

Scales of the BRIEF

Scale	Item	Total No. of Items for Parent Form
Inhibit	38, 41, 43, 44, 49, 54, 55, 56, 59, 65, 73, 78, 79, 81, 82	15
Shift	5, 6, 8, 12, 13, 23, 30, 39, 80, 84, 85	11
Emotional Control	1, 7, 20, 25, 26, 45,50, 62, 64, 70	10
Initiate	3, 10, 16, 47, 48, 61, 66, 71	8
Working Memory	2, 9, 17, 19, 24, 27, 32, 33, 37, 57, 83	11
Plan/Organize	11, 15, 18, 22, 28, 35, 36, 40, 46, 51, 53, 58, 76, 77, 86	15
Organization of Materials	4, 29, 67, 68, 69, 72, 74, 75	8
Monitor	14, 21, 31, 34, 42, 52, 60, 63	8
Total No. of Items		**86**
Validity scales		Scoring Instructions for Validity Scales
Inconsistency	(7,25), (11, 22), (27, 17), (33, 32), (38, 59), (41, 65), (42, 63), (44, 54), (53, 60), (55, 44)	For each item in a pair, obtain the score for each item, and subtract the scores, keeping the absolute difference. Sum the 10 absolute differences to get the Inconsistency score. Classification[1]: 0-6: Acceptable 7-8: Questionable

		≥9: Inconsistent
Negativity	8, 13, 23, 30, 62, 71, 80, 83, 85	Count how many of the 9 items in the scale have a score of 3. That is the negativity score. Classification[1]: 0-4 Acceptable 5-6 Elevated ≥7 Highly Elevated

To calculate the *Behavioral Regulation Index (BRI*) raw score, sum the scale raw scores obtained for Inhibit, Shift, and Emotional Control scales.
To calculate the *Metacognition Index (MI)* raw score, sum the raw scale scores obtained for Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor scales.
To calculate the Global Executive Composite (GEC) raw score, sum the raw scores for BRI and MI.

Missing data handling (For items 1-72 only; items 73-86 are additional clinical items)

1. ***If the total number of unanswered items is >14, do not compute any of the (eight) scale raw scores (INH, S, EC, INI, WM, PO, OM, m) for the BRIEF, as per the authors, the "protocol should be considered invalid". In that case, all the scale raw scores will be missing, and the index scores will be missing as well.***
2. ***If more than 2 (of the first 72) items have missing responses for a Scale (any of the 8 listed above), then a scale raw score should not be calculated. However, for any scale with 2 or fewer missing responses, impute a score of "1" for the missing item.***
3. ***IMPORTANT: When calculating index scores, please first obtain the scale raw scores, and then the index scores are derived from the scale raw scores. Do not simply add up the scores for the individual questions.***

References:

[1] Gioia GA, Espy KA, Isquith PK. BRIEF-P: Behavior Rating Inventory of Executive Function-Preschool Version. Professional Manual. 2003 Edition. Pages 15-16, Tables 2 and 4.
[2] Gioia GA, Espy KA, Isquith PK. BRIEF-P: Behavior Rating Inventory of Executive Function-Preschool Version. Professional Manual. 2003 Edition. Page 7."Missing Responses".

Programming Notes: Use the sheel for 14.4.6.1 for the following tables.

Table 14.4.6.3
Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) – Scoring summary table
Safety Population (De Novo Subjects)

Table 14.4.6.3.1
Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) – Scoring summary table
Safety Population (De Novo Subjects) (Japan)

Scales are:

Inhibit
Shift
Emotional Control (EC)
Self Monitor
Initiate
Working Memory (WM)
Plan/Organize (PO)
Organization of Materials (OM)

For Indexes Part, where we use the 90% CI for the EOS/ET measurement, the following are used, along with relevant footnotes;

Behavioral Regulation Index (BRI)[1]
Metacognition Index (MI)[2]
Global Executive Composite (GEC) [3]

For the following line, include [4] as footnote
90% CI for change from BL[4]

[1] Computed as the sum of the scale raw scores obtained for Inhibit, Shift, Emotional Control, and Self Monitor.
[2] Computed as the sum of the raw scale scores obtained for Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor.
[3] Computed as the sum of the raw scale scores for BRI and MI.
[4] Confidence interval of the mean change from baseline based on the t distribution.

Scales of the BRIEF-A

Scale	No. of items	Items	Scoring Instructions (for each individual)*
Inhibit	8	5, 16, 29, 36, 43, 55, 58, 73	Add up scores for items on the scale
Shift	6	8, 22, 32, 44, 61, 67	Add up scores for items on the scale
Emotional Control	10	1, 12, 19, 28, 33, 42, 51, 57, 69, 72	Add up scores for items on the scale
Self-Monitor	6	13, 23, 37, 50, 64, 70,	Add up scores for items on the scale
Initiate	8	6, 14, 20, 25, 45, 49, 53, 62	Add up scores for items on the scale
Working Memory	8	4, 11, 17, 26, 35, 46, 56, 68	Add up scores for items on the scale
Plan/Organize	10	9, 15, 21, 34, 39, 47, 54, 63, 66, 71	Add up scores for items on the scale
Task Monitor	6	2, 18, 24, 41, 52, 75	Add up scores for items on the scale
Organization of Materials	8	3, 7, 30, 31, 40, 60, 65, 74	Add up scores for items on the scale
Validity scales			
Infrequency		10, 27, 38, 48, 59	Number of question responses where:(Question 10 = 3), (Question 27 = 1), (Question 38 = 3), (Question 48 = 1), Question 59 = 1) Number of questions meeting conditions: 0-2 is Acceptable. >= 3 is Infrequent.
Inconsistency	10 pairs	(2, 41), (25, 49), (28, 42), (33, 72), (34, 63), (44, 61), (46, 56), (51, 75), (60, 74), (64, 70).	For each item in a pair, obtain the score for each item, and subtract the scores, keeping the absolute difference. Sum the 10 absolute differences to get the Inconsistency score.

			Classification[1]: 0-7: Acceptable ≥ 8: Inconsistent
Negativity	10	1, 8, 19, 21, 22, 23, 29, 36, 39, 40	Count the number of items with a score of 3. That is the negativity score. Classification[1]: 0-5 Acceptable ≥ 6 Elevated

2. *Missing data handling for the BRIEF-A

1. If the total number of unanswered items is >= 1 in the Shift, Self-Monitor, and Task Monitor, the raw domain score is invalidated and won't be calculated.

2. If the total number of unanswered items is >= 2 in the Inhibit, Emotional Control, Initiate, Working Memory, Plan/Organize, and Organization of Materials, the raw domain score is invalidated and won't be calculated. However, for any scale with 1 missing responses, impute a score of "1" for the missing item.

3. IMPORTANT: When calculating index scores, please first obtain the scale raw scores, and then the index scores are derived from the scale raw scores. Do not simply add up the scores for the individual questions.

LISTINGS

All listing displays for this open-label study are to be done by country and study site. Then by subject number.

Programming Note: May keep the by Treatment group, but treatment group = ZX008 OL for all subjects in this open-label study.

Listing 16.2.1.1
Subject completion/discontinuation

Subject Identifier	Country	Site/ Investigator	Withdrawal/ Completion Date/Day#	Completed as Scheduled	Reason for Premature Discontinuation*
XXXX	TEXT	XXX/TEXT	DDMMMYYYY/XX	Yes/No	Adverse Event/Serious Adverse Event Death Investigator Decision Lack of Efficacy Lost to follow-up Protocol Violation Sponsor Decision Voluntary Withdrawal Inclusion/Exclusion Criteria not met Other reason: TEXT

Relative to first dose of study treatment.
* If more than one reason is given for premature discontinuation, the first reason listed is the primary reason.

Note to Programmers: Please put the primary reason first in the list. Use the same shell for

Listing 16.2.1.2
Subject completion/discontinuation (Japan)

Listing 16.2.2.1
Major Protocol Deviations

Treatment group: xxx

Subject Identifier	Country	Site/ Investigator	Type	Major Protocol Deviation
XXXX			Inclusion/Exclusion	TEXT
			Compliance <80% or >120%	TEXT
				TEXT*
XXXX			TEXT	
XXXX				
.				
.				
.				

Programming Note: Please put the primary reason first in the list. Use the same shell for

Listing 16.2.2.2
Major Protocol Deviations (Japan)

Listing 16.2.3.1

Subjects Excluded from Analysis Populations

Subject Identifier	Deviation/Reason	Analysis Population(s) Excluded from
XXXX	TEXT	
XXXX		
XXXX		
.		
.		
.		

Programming note: ***For inclusion/exclusion criteria not met use the wording of the criteria not met from the CRF.***

Use the 16.2.3.1 shell for:

Listing 16.2.3.1.1
Subjects Excluded from Analysis Populations (Japan)

Listing 16.2.3.2
Subject allocation to trial Populations

Treatment group: xxx Country: xxxx

Subject Identifier	Site	Core Study	Enrolled population	Safety Population	mITT Population
XXXXX		VS01, VS02, 1504-C1, 1504-C2	Yes	Yes/No	Yes/No
XXXXX					
XXXXX					
.					
.					
.					

mITT = Modified Intent-to-Treat.
Note: Blank core study indicates de novo subject.

Programming note: Use the 16.2.3.2 shell for:

Listing 16.2.3.2.1
Subject allocation to trial Populations (Japan)

Listing 16.2.4.1.1
Demographic Data

Treatment group: xxx

			Date of							Baseline	Baseline	Baseline
Subject		Visit 1	Informed Consent/Assent		Date of	Age*				Weight*	Height*	BMI*
Identifier	Country	Date	Parent	Child	Birth	(years)	Sex	Race	Ethnic Group	(kg)	(m)	(kg/m^2)
XXXX	TEXT	DDMMMYYYY	DDMMMYYYY	DDMMMYYYY	DDMMMYYYY	XX	Male Female	Caucasian Black/African American Asian Pacific Islander Etc.	Latino NonLatino	XXX	XXX	XX.X
XXXX												
XXXX												
.												
.												
.												

* Age at Visit 1.

Programming note: Informed consent/assent date should be the initial consent obtained at Visit 1 of 1503 (or Visit 13 of the core study)

Use the shell for 16.2.4.1.1 for

Listing 16.2.4.1.1.1
Demographic Data (Japan)

Listing 16.2.4.1.2
% Change from baseline in weight and BMI

Treatment group: xxx

			Weight				BMI			
Subject Identifier	Visit	Date/Day	Result (kg)	Base Flag	Change from Baseline	% change from Baseline *	Result (kg/m2)	Base Flag	Change from Baseline	% change from Baseline *
1501-0101-02	Visit 1 - Day 1	ddmonyyyy/hh:mm	45.9	Y			17.17	Y		
	Visit 3 - Month 1 (Clinic)	ddmonyyyy/hh:mm	45		-0.9	-1.96	16.77		-0.4	-2.33
	Visit 4 - Month 2 (Clinic)	ddmonyyyy/hh:mm	44.59		-1.31	-2.85	16.77		-0.4	-2.33
	….									
	Visit 12 - Month 24 (Clinic)		45		-0.9	-1.96 *	16.85		-0.32	-1.86
……										

BMI = Body mass index; * Indicates a decrease from baseline in weight or BMI >= 7%.

Programming note: Use the shell for 16.2.4.1.2 for

Listing 16.2.4.1.2.1
% Change from baseline in weight and BMI (Japan)

Listing 16.2.4.2
Medical History

Treatment group: xxx

Subject Identifier	Previous or Concurrent Medical History Term/ Medical Condition/Surgical Procedure	Onset Date/Day#	Stop Date/Day#	Ongoing at Screening
XXXX	TEXT	DDMMMYYYY/XX		Ongoing
		DDMMMYYYY/XX	DDMMMYYYY/XX	Stopped
XXXX	TEXT			
XXXX				
.				
.				
.				

Relative to first dose of study treatment.

Listing 16.2.4.3
Prior and concomitant medications and therapies/treatments

Treatment group: xxx

Subject Identifier	Medication/ ATC Classification [1]	Dose	Unit	Route	Frequency*	Indication	Start Date/Day#	Stop Date/Day#
XXXX	TEXT & TEXT	TEXT	XXXX	TEXT	B1M1 BID PRN Q4H Q6H Q12H Q24H QID QM	TEXT	DDMMMYYYY/XX	DDMMMYYYY/XX Ongoing

Relative to first dose of study treatment.
* B1M1 = Twice per month, BID = Twice per day, PRN = As needed, Q4H = Every four hours, Q6H = Every Six hours, Q12H = Every Twelve hours, Q24H = Every Twenty-four hours, QID = Four times a day, QM = Every Month.
& Prior medication.
[1] WHO Drug Dictionary (latest version).
Programming note: Use the shell for 16.2.4.3 for

Listing 16.2.4.3.1
Prior and concomitant medications and therapies/treatments (Japan)

Listing 16.2.4.4.1
Prior antiepileptic Drugs (AEDs)

Subject Identifier	Medication /ATC Classification [1]	Type of treatment	Route	Dose	Frequency*	Start Date/Day#	Stop Date/Day#
XXXX	TEXT	Non-medication	TEXT	TEXT	B1M1 BID PRN Q4H Q6H Q12H Q24H QID QM	DDMMMYYYY/XX	DDMMMYYYY/XX Ongoing
	& TEXT	Risk medication					

* B1M1 = Twice per month, BID = Twice per day, PRN = As needed, Q4H = Every four hours, Q6H = Every Six hours, Q12H = Every Twelve hours, Q24H = Every Twenty-four hours, QID = Four times a day, QM = Every Month. Qd or QD=Daily, or Everyday, or once a day.
# Relative to first dose of study treatment.
& Prior medication.
[1] WHO Drug Dictionary

Programming note: **Use the shell for 16.2.4.4.1 for the following listings.**

Listing 16.2.4.4.2
Concomitant antiepileptic Drugs (AEDs)

Listing 16.2.4.4.3
Prior antiepileptic Drugs (AEDs) (Japan)

Liisting 16.2.4.4
Concomitant antiepileptic Drugs (AEDs) (Japan)

Listing 16.2.4.5
Rescue medications

Liisting 16.2.4.5.1
Rescue medications (Japan)

Listing 16.2.5.1
IMP Intake per day during Treatment

Country:

Subject Identifier	Date+Time	Study Day#	Epoch	Dose Taken? (None/Partial/Full)
XXXX				
XXXX				
.				
.				
.				

Relative to first dose of study treatment.
[1] Study date and time is the time the dose was entered into diary
[2] Study medication was administered twice daily, and compliance was recorded each time in the eDiary as full, partial or none.

Programming note: **Use the shell for 16.2.5.1 for**

Listing 16.2.5.1.1
IMP Intake per day during Treatment (Japan)

Listing 16.2.5.2
IMP Intake – self reported % compliance

Treatment group: xxx
Subject Identifier: <subject no.> Age: < > Sex:<x>

Study Week	Day1	Day2	Day3	Day4	Day5	Day6	Day7	Compliance %
1								
2								
3								
4								
Month1								Xxx.xx%
5								
6								
7								
8								
Month2								xxx.x%
…								
…..								

Note: Study medication was administered twice daily, and compliance was recorded each time in the eDiary as full, partial or none. (See Listing 16.2.5.1) From this, compliance was calculated by assuming that a missed dose=0% of dose consumed, partial=50%, full=100%.
Programming Note: from daily diary record.

Programming note: **Use the shell for 16.2.5.2 for**

Listing 16.2.5.2.1
IMP Intake – self reported % compliance (Japan)

Listing 16.2.5.3
Drug Accountability and Compliance to Study Treatment by Visit

Treatment group: xxx

Subject Identifier	Visit	Bottle Number	Amount Of volume Dispensed	Date/Day# Dispensed	Amount of Volume Returned	Date/Day# Returned
XXXX	V1, etc.	XXXXXX XXXXXX NA	XXX XXX TEXT NA	DDMMMYYYY/XX DDMMMYYYY/XX NA	NA DDMMMYYYY/XX	
XXXX						
XXXX						
.						
.						
.						

Relative to first dose of study treatment.

Programming Notes: Use 28 days, keep in ADEC. Use the shell for 16.2.5.3 for

Listing 16.2.5.3.1
Drug Accountability and Compliance to Study Treatment by Visit (Japan)

Listing 16.2.6.1
Convulsive seizure – duration and number of occurrences per subject (Diary data)

Randomized Treatment: XXX

Subject Identifier	Period	Seizure Date/Study Day**	Time of Seizure	Single/ Cluster/Discrete	Type of convulsive seizure	Duration of seizure	Approximate duration of cluster	Number of seizures
XXXX	<Baseline(Core)> <Core Study(T+M)> <OLE Treatment>	Yyyy-mm-dd Yyyy-mm-dd Yyyy-mm-dd		<Single, or Cluster>	Type 1 Type 2 Type 3 …	<2 min 2-10 min >10min		1 2 3* 4 …
XXXX								
XXXX								
.								
.								
.								

*Note: Clusters of seizures could be recorded by duration, by number of seizures, or both. When reported by duration only, the number of seizures was set equal to 3 for analysis.
**With reference to start of OLE Study

Programming note: Present the subject identifier (grayed out) on all lines after the first line for a subject.

Convulsive seizures:
A: HEMICLONIC (Note lateralization: R body, L body, or independent R and L)
B1: FOCAL WITH CLEAR OBSERVABLE MOTOR SIGNS (i.e. automatisms, dystonic posturing, focal tonic stiffening)
C: SECONDARILY GENERALIZED TONIC CLONIC (evolving to bilateral convulsive seizure from focal seizure)
D: GENERALIZED TONIC CLONIC CONVULSION
G: TONIC
I: CLONIC (Note bilateral: symmetric R and L)
J: TONIC/ATONIC (cannot differentiate) - 'drop attacks' should be placed here

Use the shell fo 16.2.6.1 for

Listing 16.2.6.1.1
Convulsive seizure – duration and number of occurrences per subject (Diary data) (Japan)

Listing 16.2.6.2
Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data)

Treatment group: XXX

Subject Identifier	Period	Seizure Date/Study Day**	Single/ Cluster	Type of non-convulsive seizure	Duration of seizure	Approximate duration of cluster	Number of seizures
XXXX	Baseline(Core) Core Study(T+M) OLE Treatment	Yyyy-mm-dd Yyyy-mm-dd Yyyy-mm-dd	<Single, or Cluster> Single, or Cluster> Single, or Cluster>	Type 1 Type 2 Type 3 …	<2 min 2-10 min >10min		1 2 3* 4 …
XXXX							
XXXX							
.							
.							
.							

*Imputed – the number of seizures in the cluster was not stated. It was imputed as 3.
**With reference to start of OLE Study.

Programming note: Present the subject identifier (grayed out) on all lines after the first line for a subject.

Non-convulsive Seizures:

B2: FOCAL WITHOUT CLEAR OBSERVABLE MOTOR SIGNS (i.e. autonomic changes like color change or pupillary dilation, and no motor signs)
E: ABSENCE OR ATYPICAL ABSENCE
F: MYOCLONIC
H: ATONIC – not resulting in a drop
K: INFANTILE SPASMS (if under 3 years of age)
L: EPILEPTIC SPASMS (if 3 years of age and older)

M: NON CONVULSIVE STATUS (greater than 30 min)
O: OTHER
Programming Note: Use the 16.2.6.2 shell for

Listing 16.2.6.2.1
Non-Convulsive seizure – by type, duration and number of occurrences per subject (Diary data) (Japan)

Listing 16.2.6.3
Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject

Treatment group: XXX

Subject Identifier	Period	Number of Days with a Seizure Occurrence	Longest interval between convulsive seizures	Convulsive seizure free days
XXXX	Baseline(Core) Core Study(T+M) OLE Treatment	Xxx Xxx xxx	xx Xxx xxx	XX Xxx xxx
XXXX				
XXXX				
.				
.				
.				

Programming Note: Present the subject identifier (grayed out) on all lines after the first line for a subject. Use the 16.2.6.3 shell for

Listing 16.2.6.3.1
Duration of the Longest interval between convulsive seizures and convulsive seizure free days per subject (Japan)

Listing 16.2.6.4
Percent reduction in convulsive seizure frequency from baseline

Treatment group: XXX

Subject ID	mITT Population?	Period	CSF per 28 Days	% Change from Baseline(Core)	>=25%? (Y/N)	>=50%? (Y/N)	>=75% (Y/N)	=100%? (Y/N)
XXXX	Y	Baseline (Core)	xxx.x					
		Core Study (T+M)	xxx.x	xxx.x	Y	N	Y	N
		Month1-EOT	xxx.x	xxx.x	Y	Y	N	N
		Month2-EOT	xxx.x	xxx.x	Y	N	N	N
XXXX	Y	Baseline (Core)	xxx.x					
		Core Study (T+M)	xxx.x	xxx.x	Y	Y	Y	N
		Month1-EOT	xxx.x	xxx.x	Y	Y	Y	N
		Month2-EOT	xxx.x	xxx.x	Y	Y	Y	N
XXXX	Y	Baseline (Core)	xxx.x					
		Core Study (T+M)	xxx.x	xxx.x	Y	Y	Y	N
		Month1-EOT	xxx.x	xxx.x	Y	Y	Y	N
XXXX	Y	Month2-EOT	xxx.x	xxx.x	Y	Y	Y	Y

Programming Note: Present the subject identifier (grayed out) on all lines after the first line for a subject.
Use the 16.2.6.4 shell for

Listing 16.2.6.4.1
Percent reduction in convulsive seizure frequency from baseline (Japan)

Listing 16.2.6.5
Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator

Subject Identifier	Age/sex	Assessment Date	Clinic Visit	Analysis Visit	CGI score by parent/caregiver	CGI score by Investigator
XXXX				Visit 1, Visit 3, Visit 4, Visit 5, Visit 6, Visit 7, Visit 8, ...	Very much improved Much improved Minimally improved No change Minimally worse Much worse Very much worse	Very much improved Much improved Minimally improved No change Minimally worse Much worse Very much worse
				Visit 12		
XXXX				...	...	...
XXXX						
.						

.
.

Note: CGI = Clinical Global Impression
Programming note: Present the subject identifier (grayed out) on all lines after the first line for a subject. Use the shell for 16.2.6.5 for

Listing 16.2.6.5.1
Clinical Global Impression – Improvement rating as assessed by the Parent/Caregiver and Investigator (Japan)

Listing 16.2.6.6
Quality of life in Childhood Epilepsy Scale

Treatment group: ZX008 OL

Subject Identifier	Age/Sex	Visit	[redacted]	Response (Raw Score)	Transformed Score
XXXX		Baseline		XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	

			[redacted]		
				XXXXX	
				XXXXX	
				XXXXX	
				XXXXX	
XXXX					

PARCAT1='QOLCE'

Listing 16.2.6.7
Quality of life of the Parent/Caregiver using EQ-5D-5L scale

Subject Identifier	Age/Sex	Visit	Assessment Date/Day #	Was the assessment done	[redacted]	Response
XXXX		Baseline	DDMMMYYYY/XX	Yes		XXXXXX
				No		XXXXXX
		End of study visit				XXXXXX
						XXXXXX
						XXXXXX
						XX
XXXX		...		...	...	
XXXX						
.						
.						
.						

Listing 16.2.6.8
Quality of life of the Parent/Caregiver using HADS scale

Subject Identifier	Visit [1]	Was the assessment done	[redacted]	Response
XXXX	Baseline Visit 1			XXXXX
				XXXXX
				XXXXX
	Visit 3			XXXXX
				XXXXX
	Visit 4			XXXXX
				XXXXX
				XXXXX
	Visit 5			XXXXX
				XXXXX
				XXXXX
	---			XXXXX
				XXXXX
				XXXXX
				XXXXX
	Visit 12			
XXXX	…	…		
XXXX				

[1] repeated for Visit 1 and each clinical visit from Visit 3 through Visit 16

Programming note: This table for ZX008 – 1501 and ZX008-1502 subjects only. Do not include ZX008-1504 Cohort 2

Listing 16.2.6.9.1
Pediatric Quality of Life Inventory (Peds QL)- for TODDLERS (age 2-4 years)

Treatment Group: ZX008 OL

Subject Identifier	Visit [1]	[redacted]	Response
			AVALC
XXXX	Baseline		XXXXX
	Visit 1		
			XXXXX
			XXXXX
	Visit 3		XXXXX
			XXXXX
			XXXXX
			XXXXX
			XXXXX
			XXXXX
	---		XXXXX
			XXXXX
			…
			…
	Visit 12		
XXXX	…		…
XXXX			
.			
.			
.			

[1] Repeated for Visit 1 and Visit 3 through Visit 16

Programming Notes: Use Listing shell 16.2.6.9 for below listings:

Listing 16.2.6.9.2
Pediatric Quality of Life Inventory (Peds QL) - for Young Children (age 5-7 years)

Listing 16.2.6.9.3
Pediatric Quality of Life Inventory (Peds QL) - for Children (age 8-12 years)

Listing 16.2.6.9.4
Pediatric Quality of Life Inventory (Peds QL) - for TEENS (age 13-18 years)

Listing 16.2.6.9.5
Pediatric Quality of Life Inventory (Peds QL) – Family Impact Module

Listing 16.2.6.10
Study Medication Palatability Assessment

Treatment Group: ZX008 OL

Subject Identifier	Age/Sex	Visit	Was the assessment done	Question	Response
XXXX		Visit 3	Yes No	1 – Over the past month, on the basis of the reaction / facial expression of your child, do you think that the medicine's taste and texture are acceptable/not acceptable to your child?	XXXXXX
				2 – Over the past month, please rate [1]how much your child likes/dislikes the medicine's taste	XXXXXX
				3 - Over the past month, do you sometimes have problems giving the medicine to your child due to its taste or texture?	XX
XXXX			…	…	
XXXX					
.					
.					
.					

[1]Rating scale: 5=likes it very much; 4=likes it; 3=neither likes or dislikes it; 2=dislikes it; 1=dislikes it very much

Listing 16.2.6.11
Sleep quality and mealtime behavior

Treatment Group: ZX008 OL

Subject Identifier	Age/Sex	Visit	Date of Assessment /Day #	Sleep Quality Question Response	Mealtime Behavior Question Response
XXXX	xxx/x	Visit 3	DDMMMYYYY/XXX	More Disturbed Same Better	Worse Behavior Not Changed Improved Behavior
XXXX				…	
XXXX					
.					
.					
.					

Note: This scale is collected only for subjects from core study ZX008-1504.
 # Relative to first dose of study treatment.

Listing 16.2.6.12
Karolinska sleepiness scale

Treatment Group: ZX008 OL

Subject Identifier	Age/Sex	Visit	Date of Assessment /Day #	[redacted]	
XXXX	xxx/x	Visit 3	DDMMMYYYY/XXX		
XXXX					
XXXX					
.					
.					
.					

Note: This scale is collected only for subjects from core study ZX008-1504.
 # Relative to first dose of study treatment.
[1] Values 1 – 6 are categorized as Alert. Values 7 – 9 are categorized as sleepy.

Listing 16.2.7.1
Adverse Events

Subject Identifier	Age/ Gender/ Race	Adverse Event (System Organ Class/ Preferred Term)	Start Date/ Day#	stop Date/ Day#	Related to study Drug	Severity	Action Taken with Study treatment	Other Action Taken	Outcome	Serious
XXXX	Xx/ X/ x	& TEXT (SOC/PT)	DDMMMYYYY /XX	DDMMMYYYY /XX	Yes No	Mild Moderate Severe	Dose not changed Dose Increased Dose reduced Drug Interrupted Drug Withdrawal NA	None withdrawn from study Treated with Medication Other: TEXT	Not resolved Resolved Resolved w/sequelae Resolving Unknown Fatal	Yes: Death Life-Threatening Hospitalization Disability/Permanent Damage Congenital Anomaly/Birth defect Medically significant No
XXXX										
XXXX										
.										
.										
.										

Relative to first dose of study treatment.
& Treatment-emergent adverse event.
NA = Not applicable

Programming note:
Use the shell for 16.2.7.1 for the following listings:
Listing 16.2.7.1.1 Adverse events (Japan)
Listing 16.2.7.2 Adverse events of special interests (AESI)
Listing 16.2.7.2.1 Adverse events of special interests (AESI) (Japan)

Note: Please record only Adverse event of special interest as per definition provided in Protocol

Listing 16.2.8.1.1
Laboratory Data: Hematology parameters

Subject Identifier	Visit	Sample Date/Day# and	Parameter	Value*	Reference Range	Unit
XXXX	Screening (Visit 1)	DDMMMYYYY/XX	Haemoglobin	XX.X H	XX.X-XX.X	TEXT
	Visit 2	ND: TEXT	Haematocrit	XX.X L		
	Visit 3		…	XX.X		
	Visit 4			…		
	Visit 5					
	Visit 6					
	…					
	Visit 12					
XXXX						
XXXX						
.						
.						
.						

ND = Not Done.
# Relative to first dose of study treatment.
* H = Above reference range, L = Below reference range

Programming Notes: Use the shell for 16.2.8.1.1 for the following listings:

Listing 16.2.8.1.1.1
Laboratory Data: Hematology parameters (Japan)

Listing 16.2.8.2.1
Laboratory Data: Biochemistry parameters

Listing 16.2.8.2.1.1
Laboratory Data: Biochemistry parameters (Japan)

Listing 16.2.8.3
Laboratory Data: Coagulation parameters

Listing 16.2.8.3.1
Laboratory Data: Coagulation parameters (Japan)

Listing 16.2.8.4.1
Laboratory Data: Urinalysis parameters

Listing 16.2.8.4.1.1
Laboratory Data: Urinalysis parameters(Japan)

For Listing 16.2.8.4 and 16.2.8.4.1, Urinalysis – add column "Result" (as 5th column) with result "Normal" or "Abnormal".

Listing 16.2.8.5
Tests of growth, precocious puberty and Thyroid Function

Listing 16.2.8.5.1
Tests of growth, precocious puberty and Thyroid Function (Japan)

Programming Notes: ***Please use STLB11 from ISS*** but only include Baseline (OLE) through End of Study in OLE for the following listngs.

Listing 16.2.8.1.2
Most Abnormal Laboratory Parameters during Open-label Treatment Period - Hematology

Listing 16.2.8.1.2 .1
Most Abnormal Laboratory Parameters during Open-label Treatment Period - Hematology ***(Japan)***

Programming Notes: Use shell for ISS STLB12 but only include Baseline (OLE) through End of Study in OLE for the following listings.

Listing 16.2.8.2.2
Most Abnormal Laboratory Parameters during Open-label Study Periods – Biochemistry

Listing 16.2.8.2.2.1
Most Abnormal Laboratory Parameters during Open-label Study Periods – Biochemistry (Japan)

Programming Notes: Please use shell for ISS Listing STLB13 but only include Baseline (OLE) through End of Study in OLE for the following listings.

Listing 16.2.8.4.2
Most Abnormal Laboratory Parameters during Open-label Study Periods -- Urinalysis

Listing 16.2.8.4.2.1
Most Abnormal Laboratory Parameters during Open-label Study Periods -- Urinalysis ***(Japan)***

Use shell from 16.2.8.2.2 – add column "Result" (as 5th column) with result.

Listing 16.2.8.6
Urine Pregnancy Test

Subject Identifier	Was Pregnancy test performed	Date of Urine pregnancy test / (Visit)	Result
XXXX	NA(female of non-child bearing potential)	DDMMMYYYY/ Visit X	Negative
	Not Done		Positive
	Done		
XXXX			
XXXX			
.			
.			
.			

Relative to first dose of study treatment.

Programming Notes: Use the shell for 16.2.8.6 for the following:

Listing 16.2.8.6.1
Urine Pregnancy Test (Japan)

Listing 16.2.8.7
Urine THC panel

Listing 16.2.8.7.1
Urine THC panel (Japan)

Listing 16.2.8.8
Whole blood cannabidiol

Listing 16.2.8.8.1
Whole blood cannabidiol (Japan)

Listing 16.2.9.1.1
Vital Signs

Treatment group: xxx

Subject Identifier	Age/Sex	Visit	Visit Date/Day#	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (bpm)	Respira-tory (Breaths/ min)	Body Weight (kg)	Body Height (cm)	BMI (kg/m^2)	Temper-ature (C)
XXXX	XX/X	Screening (Visit 1)	DDMMMYYYY/XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		Visit 2		XXX	XXX	XXX	XXX	XXX	XXX	XXX	
		Visit 3			XXX			XXX	NA	XXX	
		Visit 4		XXX	XXX	XXX	XXX	XXX	NA	XXX	
		Visit 5		XXX	XXX	XXX	XXX	XXX	NA	XXX	
		Visit 6			XXX						
		Visit 7		XXX		XXX	XXX	XXX	NA	XXX	
		Visit 8		XXX	XXX	XXX	XXX	XXX	XXX	XXX	
		.....		XXX	XXX	XXX	XXX	XXX	NA	XXX	
		Visit 16		XXX	XXX	XXX	XXX	XXX	XXX	XXX	
				XXX	XXX	XXX	XXX	XXX	XXX	XXX	
				XXX		XXX	XXX				
XXXX											
XXXX											
.											

NA = Not Applicable.
# Relative to first dose of study treatment.

Programming Note; Use shell for 16.2.9.1.1or the following listings.

Listing 16.2.9.1.1.1
Vital signs (Japan)

Listing 16.2.9.1.2
Abnormal Vital signs data (Japan)

Listing 16.2.9.1.2.1
Abnormal Vital signs data (Japan)

Programming Note : The lows and highs for determination of abnormality will be supplied by Zogenix. Abnormal weight range: subjects with weight decrease of >=7% or increase of >=7%. For these subjects, include the baseline, treatment value, change from baseline, their age and sex.

Listing 16.2.9.1.9
Subjects with Weight Decrease >5% during Treatment

Treatment Group: xxx

Subject Identifier	Age	Sex	Did Subject have a TEAE of decreased appetite? (Yes/No)*	Visit	Visit Date/Day	Weight (kg)	Baseline flag	Change From Baseline	%Change From Baseline
ZX008-1504-1001-43	13	M	No	Xxxx	16JAN2017/-109	62.69	Y		
				Xxxx	29MAY2017/25	60.33		-2.36	-3.76
				Xxxx	27JUN2017/54	38.83		-23.86	-38.06#
				Xxxx	24JUL2017/81	57.79		-4.9	-7.82
ZX008-1504-1001-45	9	M	No	Xxxx	27JAN2017/-116	22.77	Y		
				Xxxx	20JUN2017/29	21.5		-1.27	-5.58#
				Xxxx	25JUL2017/64	21.82		-0.95	-4.17
				Xxxx	18AUG2017/88	22.72		-0.05	-0.22
ZX008-1504-1001-46	16	F	No	Xxxx	25JAN2017/-124	113.76	Y		
				Xxxx	29MAY2017/1	106		-7.76	-6.82
				xxxx	27JUN2017/30	105.01		-8.75	-7.69

Programming note: use shell as used for the IDMC. Use the shell for 16.2.9.1.9 for

Listing 16.2.9.1.9.1
Subjects with Weight Decrease >5% during Treatment (Japan)

Listing 16.2.9.2
Listing of Items on Columbia-Suicide Severity Rating Scale (C-SSRS)for Individual Subjects
Safety Population

reatment	Subject number	Visit/Time-point	[redacted]	Response	Comment
XXXX	XXXXX	Visit 1,			
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX
				XXXX	XXXXXXXXXX

			[redacted]	xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				Xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
xxxx	xxxxx	Visit 3			
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx
				xxxx	xxxxxxxxxx

[redacted]

			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXXX
			XXXX	XXXXXXXXX
	…….			
XXXX	XXXXX	Visit 4, Visit 5, Visit 6, Visit 7, Visit 8…Visit 16		

Programming notes:

- List only for subjects who answered "yes" to at least one question. For those subject, list all their C-SSRS data for all time points.
- Use the 16.2.9.2 shell for

Listing 16.2.9.2.1
Listing of Items on Columbia-Suicide Severity Rating Scale (C-SSRS)for Individual Subjects (Japan)
Safety Population

Listing 16.2.9.3.1
Behavior Rating Inventory of Executive Function (BRIEF-P) Individual Responses

Randomized Treatment: XXX

Subject Identifier	Visit	Question Category	Question	Response
SUBJID	AVISITN/AVISIT	[redacted]		AVALC
XXXX	Baseline			XXXXX
	Visit 8			XXXXX
	Visit 12/EOS			XXXXX
				XXXXX
				XXXXX
				XXXXX
				XXXXX
				XXXXX
				XXXXX
				XXXXX
.				

Programming Note: Organize by items within scale scores, for all five scales.
Programming Note: provide the raw responses, not imputed responses
Programming Note: Use the shell for 16.2.9.3.1 for

Listing 16.2.9.3.1.1
Behavior Rating Inventory of Executive Function (BRIEF-P) Individual Responses (Japan)

Listing 16.2.9.3.2
Behavior Rating Inventory of Executive Function (BRIEF-P) Summary Scales

Subject Identifier	Visit	Summary Scale	Score
SUBJID	AVISITN/AVISIT	PARCATx?	AVAL
XXXX	Baseline(Core)	Inhibit	XXXXX
	Visit 12/EOS	Shift	
		Emotional Control	
		Working Memory	
		Plan/Organize	
		Inhibitory Self-Control Index (ISCI) (Inhibit + EC)[1]	
		Flexibility Index (FI) (Shift + EC)[2]	
			…
		Emergent Metacognition Index (EMI) (WM + PO)[3]	
		Global Executive Composite (GEC) (Inhibit + Shift + EC + WM + PO) [4]	
		Inconsistency Score	
		Inconsistency Classification	
			…
		Negativity Score	
		Negativity Classification	
.			

.			

Programming note: the scores take into account the algorithm for handling missing responses.

Programming Note: Organize by scales, then index, and list inconsistency and negativity last.

Programming note: Use the shell for 16.2.9.3.2 for

Listing 16.2.9.3.2.1
Behavior Rating Inventory of Executive Function (BRIEF-P) Summary Scales (Japan)

Programming Note: Use Listing shell 16.2.9.3.1 for the following listigns. Organize by items within scale scores, for all eight scales.

Listing 16.2.9.3.3
Behavior Rating Inventory of Executive Function (BRIEF) Individual Responses

Listing 16.2.9.3.3 1
Behavior Rating Inventory of Executive Function (BRIEF) Individual Responses (Japan)

Listing 16.2.9.3.5
Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) Individual Responses

Listing 16.2.9.3.5.1
Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) Individual Responses (Japan)

Footnote: OLE Last Visit = Last available measurement during the OLE study

Programming Note: Use Listing shell 16.2.9.3.2 to produce the following listings. Organize by scales, then index, and list inconsistency and negativity last.

Listing 16.2.9.3.4
Behavior Rating Inventory of Executive Function (BRIEF) Summary Scales

Listing 16.2.9.3.4.1
Behavior Rating Inventory of Executive Function (BRIEF) Summary Scales (Japan)

Listing 16.2.9.3.6
Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) Summary Scales

Listing 16.2.9.3.6.1
Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) Summary Scales (Japan)

Footnote: OLE Last Visit = Last available measurement during the OLE study

Listing 16.2.9.4
Tanner Staging

Sex: Boys

						Tanner Stage for	
Subject Identifier	Age Group	Sex [1]	Visit	Was the Exam performed	Visit Date/Day#	Genital/Breast Development [2]	Pubic Hair Growth [3]
XXXX	>7years to <=11/>11years to <=15/>15years to <=18	Male	Visit 1 Visit 3 --- Visit 8	Yes/No	DDMMMYYYY/XX	X	x
XXXX	---						
XXXX	---						
.							
.							

Relative to first dose of study treatment. [1] Table for girls registers Female in this column.
[2] Boys are rated for genital development and pubic hair growth
[3] Girls are rated for breast development and pubic hair growth

Programming Note: Use the 16.2.9.4 shell for

Listing 16.2.9.4.1
Tanner Staging (Japan)

Listing 16.2.9.5
Physical Examination

Subject Identifier	Visit [1]	Was the physical Exam performed	Visit Date/ Day #	Category	Result	Details of Abnormality
XXXX	Complete(Visit 1,Visit 8)	Yes	DDMMMYYYY/	General Appearance	Not done	TEXT
	Abbreviated(Visit 2 -7)	No	XX	Skin	Normal	
				HEENT	Abnormal	
				Respiratory		
				Abdomen		
				Cardiovascular		
				Abdomen		
				Lymph Node		
				Spine		
				Extremities		
				Other: TEXT		
XXXX						
XXXX						
.						
.						
.						

Relative to first dose of study treatment.
[1]Complete physical examination done at Visit 1 and Visit 16/ET/EOS, and at the 3 and 6 month cardiac follow-up visits; an abbreviated physical examination is done at clinic Visit 2 through Visit 16.

Programming note: Use the Listing 16.2.9.5 shell for

Listing 16.2.9.5.1
Physical Examination (Japan)

Listing 16.2.9.6
Neurological Examination

Subject Identifier	Visit [1]	Visit Date/ Day #	Was the neurological exam performed	Category	Result	Details of Abnormality
XXXX	Complete(Visit 1, Visit 8) Abbreviated(Visit 2 -7)	DDMMMYYYY/ XX	Yes No	Cranial nerves Muscle strength and tone Sensory function Coordination Gait Reflexes	Normal Abnormal	TEXT
XXXX						
XXXX						

#: Relative to first dose of study treatment.
[1]Complete neurological examination done at Visit 1 and Visit 16/ET/EOS; an abbreviated neurological examination is done at clinic Visit 2 through Visit 16.

Programming note: Use the Listing 16.2.9.6 shell for

Listing 16.2.9.6.1
Neurological Examination (Japan)