Clinical trial results:
RTG113388, a Long-term, Open-label Safety Extension Study of Retigabine/Ezogabine in Pediatric Subjects with Partial Onset Seizures (12 years old) and Subjects with Lennox-Gastaut Syndrome (12 years old)

Summary

EudraCT number	2010-020154-33
Trial protocol	Outside EU/EEA
Global end of trial date	18 June 2013

Results information

Result version number	v1 (current)
This version publication date	27 February 2016
First version publication date	27 February 2016

Trial information

Trial identification

Sponsor protocol code	RTG113388

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000116-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 June 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of retigabine/ezogabine as adjunctive treatment in subjects with either partial onset seizures (12 to <18 years old) or Lennox-Gastaut Syndrome (12 to <30 years old) who have participated in a previous ("parent") study.

Protection of trial subjects:

Subjects had standard safety testing, i.e. clinical laboratory tests, vital signs, physical examinations, and assessment of sexual maturation. To monitor for the known retigabine/ezogabine pharmacologic effects, baseline and period testing post-void residual ultrasound (urinary retention) and electrocardiogram (ECG) (QT prolongation) were required.

Weight-based dosing was implemented to ensure the exposure to retigabine/ezogabine was similar to that deemed acceptable in adults.

The suicidality risk with anti-epileptic drugs was assessed using the Columbia Suicide Severity Rating Scale (CSSR-S).

Subject study visits were to be at a similar frequency as standard care. To reduce the burden of blood sampling procedure in a population aged < 18 years, blood samples for PK analysis of retigabine/ezogabine were only taken at clinic visits concomitantly with clinical laboratory samples.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	04 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) aged 12 years or older, who had participated in a previous parent study GSK113284 (NCT014945840) evaluating Retigabine/Ezogabine in the treatment of partial onset seizures or seizures comprising Lennox-Gastaut syndrome, were enrolled in this open-label extension study.

Pre-assignment

Screening details:

Eligible par. began the Treatment Period at the eligibility assessment Visit followed by a 3-week Taper Phase, and a Follow-Up Visit within 3 days from the end of the Taper Phase. The study was prematurely discontinued after enrolling only 4 of the planned 500 par.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Retigabine/Ezogabine TID

Arm description:

Participants (par.) received retigabine/ezogabine as immediate release (IR) tablets three times a day (TID) as add-on therapy. Six dose strengths (25 milligrams(mg)/50 mg/100 mg/200 mg/300 mg/400 mg) were used. Doses may have been titrated no more frequently than once per week. Par. dose was adjusted as needed (e.g. based on: weight change due to increasing age and growth, efficacy or tolerability). Maximum doses allowed in the study were 900 mg per day (mg/day) (>50 kilogram (kg) weight) or 450 mg/day (30 to 50 kg weight) for par. aged <16 years old and the maximum doses allowed were 1200 mg/day (>50 kg weight) or 600 mg/day (30 to 50 kg weight) for par. aged >=16 years old.

Arm type	Experimental
Investigational medicinal product name	retigabine/ezogabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

retigabine/ezogabine as immediate release (IR) tablets three times a day (TID) as add-on therapy. Six dose strengths (25 milligrams (mg)/50 mg/100 mg/200 mg/300 mg/400 mg) were used. Doses may have been titrated no more frequently than once per week. Par. dose was adjusted as needed (e.g. based on: weight change due to increasing age and growth, efficacy or tolerability). Maximum doses allowed in the study were 900 mg per day (mg/day) (>50 kilogram (kg) weight) or 450 mg/day (30 to 50 kg weight) for par. aged <16 years old and the maximum doses allowed were 1200 mg/day (>50 kg weight) or 600 mg/day (30 to 50 kg weight) for par. aged >=16 years old.

Number of subjects in period 1	Retigabine/Ezogabine TID
Started	4
Completed	0
Not completed	4
Consent withdrawn by subject	1
Study Closed/Terminated	3

Baseline characteristics

Reporting groups	
Reporting group title	Retigabine/Ezogabine TID

Reporting group description:

Participants (par.) received retigabine/ezogabine as immediate release (IR) tablets three times a day (TID) as add-on therapy. Six dose strengths (25 milligrams(mg)/50 mg/100 mg/200 mg/300 mg/400 mg) were used. Doses may have been titrated no more frequently than once per week. Par. dose was adjusted as needed (e.g. based on: weight change due to increasing age and growth, efficacy or tolerability). Maximum doses allowed in the study were 900 mg per day (mg/day) (>50 kilogram (kg) weight) or 450 mg/day (30 to 50 kg weight) for par. aged <16 years old and the maximum doses allowed were 1200 mg/day (>50 kg weight) or 600 mg/day (30 to 50 kg weight) for par. aged >=16 years old.

Reporting group values	Retigabine/Ezogabine TID	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15.3		
standard deviation	± 1.5	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	3	3	
Race, Customized Units: Subjects			
White/Caucasian/European Heritage	4	4	

End points

End points reporting groups

Reporting group title	Retigabine/Ezogabine TID

Reporting group description:

Participants (par.) received retigabine/ezogabine as immediate release (IR) tablets three times a day (TID) as add-on therapy. Six dose strengths (25 milligrams(mg)/50 mg/100 mg/200 mg/300 mg/400 mg) were used. Doses may have been titrated no more frequently than once per week. Par. dose was adjusted as needed (e.g. based on: weight change due to increasing age and growth, efficacy or tolerability). Maximum doses allowed in the study were 900 mg per day (mg/day) (>50 kilogram (kg) weight) or 450 mg/day (30 to 50 kg weight) for par. aged <16 years old and the maximum doses allowed were 1200 mg/day (>50 kg weight) or 600 mg/day (30 to 50 kg weight) for par. aged >=16 years old.

Primary: Number of participants (par.) with any adverse event (AE) or serious adverse event (SAE) during the treatment period

End point title	Number of participants (par.) with any adverse event (AE) or serious adverse event (SAE) during the treatment period[1]

End point description:

An AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of the study medication, whether or not considered related to the study medication. A SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or scientific judgment was exercised in deciding whether reporting was appropriate in other situations. Please refer to the AE/SAE module for a list of non-serious AEs and SAE.

End point type	Primary

End point timeframe:

From the start of study medication until the end of Follow-Up (up to 178 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: Participants				
Any AE	4			
Any SAE	0			

Notes:

[2] - All Subjects Population: all participants who enrolled in the study.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with AEs leading to withdrawal

End point title	Number of participants with AEs leading to withdrawal[3]

End point description:

An AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of the study medication, whether or not considered related to the study medication. A SAE is

defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or scientific judgment was exercised in deciding whether reporting was appropriate in other situations. Please refer to the AE/SAE module for a list of non-serious AEs and SAE.

End point type	Primary

End point timeframe:

From the start of study medication until the end of the Follow-Up Visit (up to 178 days)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[4]			
Units: Participants	0			

Notes:

[4] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with vital signs outside the pre-determined clinically important findings or outside the normal ranges at any time during the study

End point title	Number of participants with vital signs outside the pre-determined clinically important findings or outside the normal ranges at any time during the study[5]

End point description:

Vital sign assessment included systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate and body temperature measurements. SBP, DBP and heart rate were measured at the following Visits: 1, 4, 5, 6, 7, EW and the FU Visit after the participants were in the seated position for 5 minutes.

End point type	Primary

End point timeframe:

Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[6]			
Units: Participants	0			

Notes:

[6] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in SBP and DBP at the indicated time points

End point title	Change from Baseline in SBP and DBP at the indicated time points[7]

End point description:

Vital sign assessment included SBP and DBP measurements. SBP and DBP were measured at the following Visits: 1, 4, 5, 6, 7, EW, and the FU Visit after the participant was in seated position for 5 minutes. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)	()			

Notes:

[8] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in heart rate at the indicated time points

End point title	Change from Baseline in heart rate at the indicated time

End point description:

Vital sign assessment included heart rate measured at the following Visits: 1, 4, 5, 6, 7, EW, and the FU Visit after the participant was in seated position for 5 minutes. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: Beats per minute (bpm)				
arithmetic mean (standard deviation)	()			

Notes:

[10] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body temperature at the indicated time points

End point title	Change from Baseline in body temperature at the indicated time points[11]

End point description:

Vital sign assessment included body temperature measurements at the following Visits: 1, 4, 5, 6, 7, EW, and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: Celsius				
arithmetic mean (standard deviation)	()			

Notes:

[12] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body height at indicated time points

End point title	Change from Baseline in body height at indicated time

End point description:

Body height was measured without shoes and wearing light clothing at the following Visits: 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[14]			
Units: Centimeter (cm)				
arithmetic mean (standard deviation)	()			

Notes:

[14] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body weight at the indicated time points

End point title	Change from Baseline in body weight at the indicated time points[15]

End point description:

Body weight was measured without shoes and wearing light clothing at the following Visits: 1, 4, 5, 6, 7, EW and FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	()			

Notes:

[16] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body mass index (BMI) at the indicated time points

End point title	Change from Baseline in body mass index (BMI) at the indicated time points[17]

End point description:

BMI is calculated as weight in kilograms (kg) divided by the square of their height in metres (m^2). BMI was measured at the following Visits: 1, 4, 5, 6, 7, EW and FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: kilogram per meter square (kg/m^2)				
arithmetic mean (standard deviation)	()			

Notes:

[18] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in electrocardiogram (ECG) at the indicated time points

End point title	Change from Baseline in electrocardiogram (ECG) at the indicated time points[19]

End point description:

The 12-lead ECG was recorded in a supine position at the Eligibility Assessment Visitand the EW Visit after having kept a participant at rest in this position for 10 minutes. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), EW Visit (up to 178 days)

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: Milliseconds				
arithmetic mean (standard deviation)	()			

Notes:

[20] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal clinically significant ECG findings based on investigator judgment at anytime during the study

End point title	Number of participants with abnormal clinically significant ECG findings based on investigator judgment at anytime during the study[21]

End point description:

The 12-lead ECG was recorded in a supine position at the Eligibility Assessment Visit andthe EW Visit after having kept a participant at rest in this position for 10 minutes. Abnormal findings were analyzed as clinically significant (CS) and not clinically significant (NCS). The study investigator judged the ECG abnormailities as CS or NCS.

End point type	Primary

End point timeframe:

Eligibility Assessment and EW Visit

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[22]			
Units: Participants	0			

Notes:

[22] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in ALT, ALP, AST, CK, and LDH measurements at the indicated time points

End point title	Change from Baseline in ALT, ALP, AST, CK, and LDH measurements at the indicated time points[23]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Alanine amino transferase (ALT), alkaline phosphotase (ALP), aspartate amino transferase (AST), creatine kinase (CK), and lactate dehydrogenase (LDH) parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and

Follow-Up (FU) Visit (up to 178 days)

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[24]			
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)	()			

Notes:

[24] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in albumin, total protein, hemoglobin, and mean corpuscle hemoglobin measurements at the indicated time points

End point title	Change from Baseline in albumin, total protein, hemoglobin, and mean corpuscle hemoglobin measurements at the indicated time points[25]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Albumin, total protein, hemoglobin, and mean corpuscle hemoglobin concentration parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[26]			
Units: Grams per Liter (G/L)				
arithmetic mean (standard deviation)	()			

Notes:

[26] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the BUN/Creatinine and the Urine Albumin/Creatinine Ratios at the indicated time points

End point title	Change from Baseline in the BUN/Creatinine and the Urine Albumin/Creatinine Ratios at the indicated time points[27]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Blood Urea Nitrogen (BUN)/Creatinine and Urine Albumin/Creatinine were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[28]			
Units: Ratio				
arithmetic mean (standard deviation)	()			

Notes:

[28] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in calcium, carbon dioxide content/bicarbonate, chloride, cholesterol, glucose, magnesium, inorganic phosphorus, potassium, sodium, and urea/BUN measurements at the indicated time points

End point title	Change from Baseline in calcium, carbon dioxide content/bicarbonate, chloride, cholesterol, glucose, magnesium, inorganic phosphorus, potassium, sodium, and urea/BUN measurements at the indicated time points[29]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Calcium, carbon dioxide content/bicarbonate, chloride, cholesterol, glucose, magnesium, inorganic phosphorus, potassium, sodium, and urea/BUN parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[30]			
Units: Millimole per liter (MMOL/L)				
arithmetic mean (standard deviation)	()			

Notes:

[30] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in creatinine, direct bilirubin, indirect bilirubin, total bilirubin, uric acid, and urine creatinine concentration measurements at the indicated time points

End point title	Change from Baseline in creatinine, direct bilirubin, indirect bilirubin, total bilirubin, uric acid, and urine creatinine concentration measurements at the indicated time points[31]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Creatinine, direct bilirubin, indirect bilirubin, total bilirubin, uric acid, and urine creatinine concentration parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[32]			
Units: Micromole per liter (UMOL/L)				
arithmetic mean (standard deviation)	()			

Notes:

[32] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Thyroid Stimulating Hormone (TSH) and Urine Albumin measurements at the indicated time points

End point title	Change from Baseline in Thyroid Stimulating Hormone (TSH) and Urine Albumin measurements at the indicated time points[33]

End point description:

Clinical laboratory assessments included measurements of endocrine and urinalysis parameters. TSH and urine albumin parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from

Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[34]			
Units: Milliunits per liter (MU/L)				
arithmetic mean (standard deviation)	()			

Notes:

[34] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, platelet count, segmented neutrophils, total neutrophils, and white blood cell count measurements at the indicated time points

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, platelet count, segmented neutrophils, total neutrophils, and white blood cell count measurements at the indicated time points[35]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Basophils, eosinophils, lymphocytes, monocytes, platelet count, segmented neutrophils, total neutrophils (Total absolute neutrophil count- total ANC), and white blood cell count parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[36]			
Units: Giga (10^9) per liter (GI/L)				
arithmetic mean (standard deviation)	()			

Notes:

[36] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, platelet count, segmented neutrophils, total neutrophils, and red cell distribution width (RDW) percentages at the indicated time points

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, platelet count, segmented neutrophils, total neutrophils, and red cell distribution width (RDW) percentages at the indicated time points[37]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Basophils, eosinophils, lymphocytes, monocytes, segmented neutrophils, total neutrophils and red cell distribution width (RDW) parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[38]			
Units: percentage (%)				
arithmetic mean (standard deviation)	()			

Notes:

[38] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the hematocrit measurements at the indicated time points

End point title	Change from Baseline in the hematocrit measurements at the indicated time points[39]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Hematocrit was measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study

was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[40]			
Units: one unit				
arithmetic mean (standard deviation)	()			

Notes:

[40] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the mean corpuscle volume and mean platelet volume measurements at the indicated time points

End point title	Change from Baseline in the mean corpuscle volume and mean platelet volume measurements at the indicated time points[41]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Mean corpuscle volume and mean platelet colume parameters were measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[42]			
Units: femtoliters (FL)				
arithmetic mean (standard deviation)	()			

Notes:

[42] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean corpuscle hemoglobin at the indicated time points

End point title	Change from Baseline in mean corpuscle hemoglobin at the indicated time points[43]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. Mean corpuscle hemoglobin was measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[44]			
Units: picograms (PG)				
arithmetic mean (standard deviation)	()			

Notes:

[44] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the red blood cell count measurements at the indicated time points

End point title	Change from Baseline in the red blood cell count measurements at the indicated time points[45]

End point description:

Clinical laboratory assessments included hematology, chemistry and urinalysis parameters. The red blood cell count was measured at Visits 1, 4, 5, 6, 7, EW and the FU Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[45] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[46]			
Units: 10^12				
arithmetic mean (standard deviation)	()			

Notes:

[46] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with hematology, chemistry and urinalysis parameters outside the normal ranges and pre-determined clinically important ranges

End point title	Number of participants with hematology, chemistry and urinalysis parameters outside the normal ranges and pre-determined clinically important ranges[47]

End point description:

Clinical laboratory assessment included hematology, chemistry and urinalysis parameters. Clinical laboratory parameters were measured at Visit 1, 4, 5, 6, 7, EW and FU Visit. Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Eligibility Assessment (Visit 1), Visit 4, Visit 5, Visit 6, Visit 7, Early Withdrawal (EW) Visit, and Follow-Up (FU) Visit (up to 178 days)

Notes:

[47] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[48]			
Units: Participants				

Notes:

[48] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Changes from Baseline in bladder volume as assessed by the post void residual (PVR) ultrasound at the indicated time points

End point title	Changes from Baseline in bladder volume as assessed by the post void residual (PVR) ultrasound at the indicated time points[49]

End point description:

The PVR urine test measured the amount of urine left in the bladder after urination. The PVR bladder ultrasound was performed by an urologist, a qualified technician or by an appropriately trained qualified study nurse at Visits 1, 6, and the EW Visit. Change from Baseline was calculated by subtracting the Baseline value from the individual post-dose values. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1), Visit 6, EW Visit

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[50]			
Units: Milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[50] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Changes from Baseline in cognition as measured by the Leiter-R at the indicated time points

End point title	Changes from Baseline in cognition as measured by the Leiter-R at the indicated time points[51]

End point description:

The Leiter International Performance Scale or simply Leiter is an intelligence test for children and adolescents, with norms ranging from 2 to 20 years. For all ages, it yields an intelligence quotient (IQ) and a measure of logical ability. It is comprised of ten subtests, seven of which were relevant to the 12-18 years age group. The administration time was approximately 40 minutes. During the study, only the parent/caregiver completed this questionnaire while the participants were within the age range (i.e. <20 years). Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). The parent study did not measure baseline cognition, behavior, and learning so changes from baseline were not available for participants in this study.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

Notes:

[51] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[52]			
Units: Scores on scale				
number (not applicable)				

Notes:

[52] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Changes from Baseline in behaviour as measured by the child behavior checklist (CBCL) at the indicated time points

End point title	Changes from Baseline in behaviour as measured by the child behavior checklist (CBCL) at the indicated time points[53]

End point description:

The CBCL is a widely used parent report questionnaire identifying behavioural and emotional problems in children. The checklist is comprised of a number of statements about the child's behavior, e.g. acts too young for his/her age. Responses were recorded on a likert scale: 0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true. The preschool checklist contained 100 questions and the school-age checklist contained 120 questions. During the study, only the parent/caregiver completed this questionnaire while the participants were within the age range (i.e. <18 years). Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). The parent study did not measure baseline cognition, behavior, and learning so changes from baseline were not available for participants in this study.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

Notes:

[53] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[54]			
Units: Scores on scale				
number (not applicable)				

Notes:

[54] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Changes from Baseline in learning as measured by the wide range assessment of memory and learning , 2nd edition (WRAML2) at the indicated time points

End point title	Changes from Baseline in learning as measured by the wide range assessment of memory and learning , 2nd edition (WRAML2) at the indicated time points[55]

End point description:

The WRAML2 is a standardized test that measures an individual’s memory functioning. It evaluates both visual and verbal, immediate and delayed memory ability along with the acquisition of new learning. The WRAML2 core battery is composed of two verbal, two visual, and two attention concentration subtests, yielding a verbal memory index, a visual memory index and an attention-concentration index. Together, these tests yield the general memory index. The administration time is approximately 40 minutes. During the study, this test was administered if the participant was within the age range (i.e. >9 years). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). The parent study did not measure Baseline cognition, behavior, and learning so changes from Baseline were not available for participants in this study.

End point type	Primary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

Notes:

[55] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[56]			
Units: Scores on scale				
number (not applicable)				

Notes:

[56] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with sexual maturation based on the Tanner Stage I to Stage V of Puberty in participants <=18 years old throughout the study

End point title	Number of participants with sexual maturation based on the Tanner Stage I to Stage V of Puberty in participants <=18 years old throughout the study[57]

End point description:

The number of participants who advanced a stage between the eligibility visit and the EW Visit was recorded. Tanner stage I is defined as no pubic hair at all (prepubertal Dominic state); stage II is defined as a small amount of long, downy hair with slight pigmentation at the base of the penis and scrotum (males) or on the labia majora (females); stage III is defined as when the hair becomes more coarse and curly, and begins to extend laterally; stage IV is defined as adult-like hair quality, extending across pubis but sparing medial thighs; and stage V is defined as when the: hair extends to medial surface of the thighs. The investigator assessed the participant's sexual development in participants <18 years old based on the Tanner Stages of Puberty.

End point type	Primary

End point timeframe:

Eligibility Assessment (Visit 1) and EW Visit

Notes:

[57] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[58]			
Units: Participants				
Stage I to Stage II	0			
Stage II to Stage III	0			
Stage III to Stage IV	0			
Stage IV to Stage V	2			
Stage V	2			

Notes:

[58] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of days of exposure to Retigabine/Ezogabine TID by individual participant

End point title	Number of days of exposure to Retigabine/Ezogabine TID by individual participant[59]

End point description:

Total number of days each participant was exposed to Retigabine/Ezogabine are recorded here.

End point type	Primary

End point timeframe:

Treatment Phase plus Taper Phase (up to 97 days)

Notes:

[59] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was conducted; thus, there are no statistical data to report

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	4[60]			
Units: Days				
Participant 1	133			
Participant 2	213			
Participant 3	196			
Participant 4	166			

Notes:

[60] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in the seizure frequency at the indicated time points

End point title	Percent change from Baseline in the seizure frequency at the indicated time points

End point description:

The percentage reduction from Baseline in the seizure frequency was summarized using descriptive statistics. The frequencies and percentages were computed for a reduction in seizure frequency of >50% as well as for a 100% reduction (seizure-free). Increases of >50% in seizure frequency was also summarized. The percentage of seizure-free days wasere also analyzed. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[61]			
Units: Percentage of seizure frequency				
arithmetic mean (standard deviation)	()			

Notes:

[61] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who were responders during the treatment period

End point title	Number of participants who were responders during the treatment period

End point description:

A ''responder'' is defined as >50% reduction from Baseline in the seizure frequency. Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[62]			
Units: Participants				

Notes:

[62] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression- Improvement (CGI-I) Assessment at the indicated time points

End point title	Clinical Global Impression- Improvement (CGI-I) Assessment at the indicated time points

End point description:

The Clinical Global Impression (CGI) scale provided an overall clinician-determined summary measure. It had 2 components: the CGI-Severity of Illness (CGI-S) scale and the CGI- Improvement (CGI-I) scale which rated the change from Baseline. The CGI-I scale scores range from 0 to 7 and are interpreted as 0=not assessed, 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, 7=very much worse. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[63]			
Units: Scores on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[63] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Severity of illness (CGI-S) assessment at the indicated time points

End point title	Clinical Global Impression-Severity of illness (CGI-S) assessment at the indicated time points

End point description:

The Clinical Global Impression (CGI) scale provided an overall clinician-determined summary measure. It had 2 components: the CGI-Severity of Illness (CGI-S) scale and the CGI-Improvement (CGI-I) scale which rated the change from Baseline. The CGI-S was a 7-point scale that required the investigator to rate the severity of the participant's epilepsy relative to the investigator's past experience with other participants with the same diagnosis. The CGI-S scale scores range from 0 to 7 and are interpreted as 0=not assessed, 1=normal, 2=borderline, 3=mild, 4=moderate, 5=marked, 6=severe, 7=extremely severe. Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline, Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[64]			
Units: Scores on scale				
arithmetic mean (standard deviation)	()			

Notes:

[64] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in child health status as measured by the child health questionnaire (CHQ) in participants <18 years old at the indicated time points

End point title	Change from Baseline in child health status as measured by the

	child health questionnaire (CHQ) in participants <18 years old at the indicated time points

End point description:

The CHQ comprises scales specifically developed for children and adolescents aged five years and older. The CHQ assesses a child's physical, emotional, and social well-being from the perspective of a parent or guardian. The questionnaire was completed by a parent/caregiver and administration time was approximately 30 minutes. The parent/caregiver completed this questionnaire while the participant was within the age range (i.e. <18 years). Baseline was the first pre-Retigabine assessment conducted in the parent study GSK113284 (NCT014945840). Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline, Eligibilty Assessment (Visit 1), EW Visit and FU Visit (up to 178 days)

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[65]			
Units: Scores on scale				
arithmetic mean (standard deviation)	()			

Notes:

[65] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve (AUC) following oral administration of Retigabine/ezogabine at the indicated time points

End point title	Area under the plasma concentration-time curve (AUC) following oral administration of Retigabine/ezogabine at the indicated time points

End point description:

AUC is defined as the area under the plasma drug concentration-time curve, reflects the actual body exposure to drug after administration of a dose of the drug and is expressed in milligram*hour per Liter (mg*h/L). Blood samples for population PK analysis of retigabine/ezogabine were taken at clinic visits where routine clinical laboratory samples were also taken. Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[66]			
Units: mg*h/L				
geometric mean (confidence interval 95%)	(to)			

Notes:

[66] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) following oral administration of Retigabine/ezogabine at indicated time points

End point title	Apparent clearance (CL/F) following oral administration of Retigabine/ezogabine at indicated time points

End point description:

Blood samples for population pharmacokinetic analysis of retigabine/ezogabine were taken at clinic visits where routine clinical laboratory samples were also taken. CL/F, where CL is the calculated as dose/AUC and F is the oral bioavailability of the drug. Because the study was terminated prematurely and the sample size is small, summary statistics were not compiled

End point type	Secondary

End point timeframe:

Eligibility Assessment (Visit 1) up to 178 days

End point values	Retigabine/Ezogabine TID			
Subject group type	Reporting group			
Number of subjects analysed	0[67]			
Units: Milliliters per hour (mL/hr)				
geometric mean (confidence interval 95%)	(to)			

Notes:

[67] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse event (AE) and serious adverse events (SAE) were collected from the start of study treatment until the Follow-Up contact (Up to 178 days)

Adverse event reporting additional description:

SAEs and non-serious AEs are reported for members of the Safety Population, comprised of participants who took at least one dose of investigational product after being enrolled into the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Retigabine/ezogabine TID

Reporting group description:

Par. received retigabine/ezogabine as IR tablets TID as add-on therapy. Six dose strengths (25 mg/50 mg/100 mg/200 mg/300 mg/400 mg) were used. Doses may have been titrated no more frequently than once per week. Par. dose was adjusted as needed (e.g. based on: weight change due to increasing age and growth, efficacy or tolerability) over the course of this long-term open-label extension study. Physicians used their clinical judgment in making dose adjustments. Maximum doses allowed in the study were 900 mg/day (>50 kilogram (kg) weight) or 450 mg/day (30 to 50 kg weight) for par. aged <16 years old and the maximum doses allowed were 1200 mg/day (>50 kg weight) or 600 mg/day (30 to 50 kg weight) for par. aged >=16 years old.

Serious adverse events	Retigabine/ezogabine TID		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Retigabine/ezogabine TID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Headache			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Ingrowing nail subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Infections and infestations Viral infection subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2011	Amendment No.01: The amendment updates the Sponsor Information, removes the Transition Phase, clarifies the population, updates the Study Design (assessments, visit schedules, definitions, and endpoints), adds the maximum daily dose, and updates the statistical section.
02 December 2011	Amendment No. 02: The amendment clarifies the differences in maximum daily dose by age, removes the expedited reporting requirement for neutrophil counts, all discontinuations due to hematological reasons/infections and all serious hematological events/infections, and includes additional assessments during Year 2 and beyond.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported