Protocol Registration Receipt
05/01/2014

Grantor: CDER IND/IDE Number: 53,950 Serial Number:

Dose-Optimization, Adjunctive Treatment Study of Ezogabine/Retigabine Immediate Release in Partial-onset Seizures

This study has been terminated.

(After reevaluation of the benefit: risk profile of ezogabine/retigabine, GSK does not believe the early adjunctive treatment study population is appropriate.)

Sponsor:	GlaxoSmithKline
Collaborators:	Valeant Pharmaceuticals International, Inc.
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT01721317

Purpose

This is a Phase IV adjunctive treatment dose-optimization study evaluating the efficacy, safety, and health outcomes of ezogabine/retigabine immediate release (IR) (GW582892) compared with placebo in adult subjects with partial-onset seizures (POS). This randomized, double-blind, placebo-controlled, parallel-group, multicenter study will compare ezogabine/retigabine IR (investigator-selected daily doses of 600 milligram (mg)/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day) with placebo. Study drug will be taken three times a day (TID) in equally or unequally divided doses.

The study design includes up to a 10-week (wk) Screening (≤2 wks)/Baseline (8 wks) Phase, a Titration Phase (2 wks), Dose-Optimization Phase (8 wks), Maintenance Phase (8 wks), and Taper/Follow-Up Phase (3 wks). The total duration of the study for each subject will be approximately 31 wks, and at minimum approximately 27 wks if subjects provide reliable 28-day retrospective seizure data.

Approximately 280 subjects will be screened with approximately 208 subjects randomly assigned to 1 of 2 treatment groups in a 2:1 ratio (ezogabine/retigabine IR, or placebo).

Subjects will be instructed to start investigational product (IP) the day after the baseline visit. During the first week of the Titration Phase, subjects will be taking 300 mg/day (100 mg TID). During the second week, subjects will be taking 450 mg/day (150 mg/day TID).

At the beginning of the Dose-Optimization Phase (3rd week of study drug) subjects will take 600 mg/day (200 mg TID) for one week. Thereafter during the Dose-Optimization Phase, subjects will continue to increase their daily dose by 150 mg per week until they have achieved their optimal tolerated dose. During this phase, the investigator may choose to have the subject stay on his/her designated dose for another week before attempting a dose increase until reaching a dose of 1200 mg/day. In addition, in the context of tolerability issues, the subject may be reduced to the preceding dose level for one week before attempting to increase the dose again at the next scheduled time point until the subject reaches optimal dose. Subjects unable to tolerate a minimum of 600 mg/day will be discontinued from the study.

The Maintenance Phase will begin at Week 10 (Visit 8) and will last 8 weeks. During the Maintenance Phase, subjects will remain on the daily TID dose achieved at the end of the Dose-Optimization Phase.

Seizure type and frequency will be monitored throughout the study via a Seizure Calendar and will be evaluated at each study visit. Subjects will be instructed to complete the daily Seizure Calendar during each phase of the study.

Condition	Intervention	Phase
Seizures	Drug: Ezogabine/Retigabine IR Drug: Placebo	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study
Official Title: Study PTG116878, a Dose-Optimization Study of Ezogabine/Retigabine Immediate Release Tablets Versus Placebo in the Adjunctive Treatment of Subjects With Partial-Onset Seizures

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Percent Change in the 28-day Total Partial Seizure Frequency (POS) From Week 0 (End of Baseline Phase) Through Week 18 (End of Maintenance Phase) [Time Frame: Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

The efficacy of ezogabine/retigabine IR as an adjunctive treatment was to be evaluated by the percent change in the total partial seizure frequency, which was recorded by participants in the daily seizure calendar. The total 28-day POS rate is defined as the total number of POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Percent Change in the 28-day Total Partial Seizure Frequency (POS) Within Each Stratum From Week 0 (End of Baseline Phase) Through Week 18 (End of Maintenance Phase) [Time Frame: Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The percent change in 28-day total POS frequency within each stratum (sodium channel blocker or non-sodium channel blocker) background antiepileptic drug (AED) was to be summarized as the supportive analysis. The total 28-day POS value is defined as the total number of POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

Secondary Outcome Measures:

- Percent Change in 28-day Total Partial Seizure Frequency (POS) for the Indicated Intervals: Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase [Time Frame: Week 3 (start of Dose -Optimization Phase) to Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The efficacy of ezogabine/retigabine IR as an adjunctive treatment was to be evaluated by the percent change in total partial seizure frequency during the Dose-Optimization Phase and Maintenance Phase. The total 28-day POS value is defined as the total number of POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Number of Par. Experiencing >=50% Reduction in 28-day Total Partial Seizure Frequency (POS) for the Intervals: Double-blind Period (Titration Phase + Dose-Optimization Phase + Maintenance Phase), Maintenance Phase and Dose-Optimization + Maintenance Phase [Time Frame: Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  Participants (par.) experiencing >= 50% reduction from Baseline to the end of the Double-Blind Phase in 28-day total POS were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Number of Seizure Free Participants for the Indicated Intervals: Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase [Time Frame: Week 3 (start of Dose-Optimization Phase) to Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  Participants without seizures during the interval of Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Change From Baseline in the Number of Seizure Free Days for the Indicated Intervals: Double-blind Period (Titration Phase + Dose-Optimization Phase + Maintenance Phase), Maintenance Phase and the Dose-Optimization + Maintenance Phase [Time Frame: Week 0 (end of Baseline Phase) to Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The change in number of seizure free days during the Double-Blind period, the Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Percent Change From Baseline in Functional Status (Epilepsy-related Worry and Activity Limitation) and Productivity (Missed Work or School) to the End of the Dose-Optimization Phase and the End of the Maintenance Phase [Time Frame: Week 3 (start of Dose -Optimization Phase) to Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The effect of ezogabine/retigabine IR as an adjunctive treatment on health outcomes was to be evaluated on the basis of functional status and productivity. Participants were asked to complete the paper functional status diary to collect information to assess how the participant's functional status is affected by their epilepsy symptoms. Participants were asked to rate their epilepsy-related worry, activity limitations, and productivity (missed work or school). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Incidence of New Seizure Types in Participants Without a History of These Seizure Types [Time Frame: Week 0 (end of Baseline Phase) to Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the incidence of new seizure types in participants without a history of these seizure types. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Number of Participants at Each Dose During the Maintenance Phase and Average Maintenance Dose Over All Participants [Time Frame: Week 11 (start of Maintenance Phase) to Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the number of participants at each dose during the Maintenance Phase and the average maintenance dose over all participants. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Number of Participants With Early Study Discontinuation [Time Frame: Week 0 (end of Baseline Phase) to Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the incidence of participants with early study discontinuation.
- Change From Baseline in Body Weight [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  Change from Baseline in body weight was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  Change from Baseline in blood pressure was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Heart Rate [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  Change from Baseline in heart rate was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in the QT Interval Using Bazett's Correction (QTcB) and QT Interval Using Fridericia's Correction (QTcF) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

Change from Baseline in the QT interval using Bazett's correction (QTcB) and QT interval using Fridericia's correction were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Change From Baseline in the Percentage of Basophils, Eosinophils, Lymphocytes, Monocytes, Neutrophils, Segmented Neutrophils and Red Blood Cell (RBC) Distribution Width [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in the Basophils, Eosinophils, Lymphocytes, Monocytes, Neutrophils, Segmented Neutrophils, White Blood Cell (WBC) Count and Platelet Count [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Hemoglobin and Mean Corpuscle Hemoglobin Concentration [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Hematocrit [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Red Blood Cell (RBC) Count [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Mean Corpuscle Hemoglobin [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Albumin and Total Protein [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Creatine Kinase, Lactate Dehydrogenase and Gamma Glutamyltransferase (GGT) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

- Change From Baseline in Direct Bilirubin, Indirect Bilirubin, Total Bilirubin, Uric Acid and Creatinine [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Calcium, Chloride, Potassium, Sodium, Glucose, Magnesium, Phosphorus Inorganic, Bicarbonate and Urea/Blood Urea Nitrogen (BUN) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in BUN/Creatinine Ratio [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated chemistry tests was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Creatinine Clearance [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated chemistry test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Urine Specific Gravity (USG) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated urinalysis test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Urine Potential of Hydrogen (pH) [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the indicated urinalysis test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize ot evaluate this endpoint.
- Number of Participants for the Indicated Urinalysis Parameters Tested by Dipstick [Time Frame: Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)] [Designated as safety issue: No]

  The change from Baseline in the following urinalysis parameters (urine occult blood, urine glucose, urine ketones and urine protein) were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
- Change From Baseline in Post-void Residual (PVR) Urinary Bladder Ultrasound Volume [Time Frame: Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase) and Week 18 (end of Maintenance Phase)] [Designated as safety issue: No]

  The change from Baseline in the PVR bladder ultrasound results was to be assessed. Due to the study being prematurely terminated, there was not

sufficient data to summarize or evaluate this endpoint.

- Number of Participants With the Indicated Assessment Events of Suicidal Behavior, Suicidal Ideation or Non-suicidal Self Injurious Behavior Via the Columbia Suicide Severity Rating Scale (C-SSRS) [Time Frame: Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 4, Week 6 and Week 8] [Designated as safety issue: No]

  Prospective assessment of suicidality was conducted using the Columbia-Suicide Severity Rating Scale (C-SSRS), a brief questionnaire designed to assess severity and change in suicidality by integrating both behavior and ideation using a semi-structured interview to probe participant responses. C-SSRS data were only collected through Week 8 for the 6 randomized participants. Due to the study being prematurely terminated, there was not sufficient data to evaluate this endpoint.

Enrollment: 6
Study Start Date: December 2012
Study Completion Date: June 2013
Primary Completion Date: June 2013

Arms	Assigned Interventions
Experimental: Titration Phase: Ezogabine/Retigabine 300 mg Subjects receive Ezogabine/Retigabine 300 mg equally divided TID over Wk 1	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Titration Phase: Placebo 300 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Titration Phase: Ezogabine/Retigabine 450 mg Subjects receive Ezogabine/Retigabine 450 mg equally divided TID over Wk 2	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Titration Phase: Placebo 450 mg	Drug: Placebo Matching placebo will be available

Arms	Assigned Interventions
Subjects receive matching Placebo	
Experimental: Dose-Optimization Phase: Ezogabine/Retigabine 600 mg Subjects receive Ezogabine/Retigabine 600 mg equally divided (200 mg TID) over Wk 3 or until they achieve their optimal tolerated dose as assessed by the Investigator	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Dose-Optimization Phase: Placebo 600 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Dose-Optimization Phase: Ezogabine/Retigabine 750 mg Subjects receive Ezogabine/Retigabine 750 mg equally or unequally divided TID over Wk 4 or until they achieve their optimal tolerated dose as assessed by the Investigator	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Dose-Optimization Phase: Placebo 750 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Dose-Optimization Phase: Ezogabine/Retigabine 900 mg Subjects receive Ezogabine/Retigabine 900 mg equally or unequally divided TID over Wk 5 or until they achieve their optimal tolerated dose as assessed by the	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.

Arms	Assigned Interventions
Investigator	
Placebo Comparator: Dose-Optimization Phase: Placebo 900 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Dose-Optimization Phase: Ezogabine/Retigabine 1050 mg Subjects receive Ezogabine/Retigabine 1050 mg equally or unequally divided TID over Wk 6 or until they achieve their optimal tolerated dose as assessed by the Investigator	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Dose-Optimization Phase: Placebo 1050 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Dose-Optimization Phase: Ezogabine/Retigabine 1200 mg Subjects receive Ezogabine/Retigabine 1200 mg equally divided (400 mg TID) over Wk 7 or until they achieve their optimal tolerated dose as assessed by the Investigator	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200 mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Dose-Optimization Phase: Placebo 1200 mg Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available
Experimental: Maintenance Phase:Ezogabine/Retigabine	Drug: Ezogabine/Retigabine IR Subjects received drug (dose strength 300 mg to 1200

Arms	Assigned Interventions
Subjects receive Ezogabine/Retigabine at the daily dose achieved (equally or unequally divided TID) at the end of the Dose-Optimization Phase for 8 Weeks (600 mg, 750 mg, 900 mg, 1050 mg, or 1200 mg)	mg) orally with or without food. The 3 daily doses are to be administered with approximately an 8-hour interval between them.
Placebo Comparator: Maintenance Phase: Placebo Subjects receive matching Placebo	Drug: Placebo Matching placebo will be available

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts healthy volunteers.

Inclusion Criteria:

- A male or female of 18 years of age or above capable of giving written informed consent
- Have a confident diagnosis of epilepsy for >=6 months with partial-onset seizures (POS), i.e., simple or complex POS with or without secondary generalization (classified according to the International League Against Epilepsy (ILAE) Guidelines, prior to the Screening Visit
- Currently receiving monotherapy treatment with an antiepileptic drug (AED) at a stable dose for at least 28 days prior to the screening visit (Visit 1). If the subject is taking a barbiturate (e.g., phenobarbital), the dose must be stable for ≥3 months prior to the Screening Visit. Note: Subjects who have received previous adjunctive treatment but are currently taking one AED are eligible for enrolment.
- Investigator-confirmed partial seizure frequency rate of ≥3 partial seizures per 28 days over the 8 weeks preceding the screening visit and must not have been seizure-free for ≥ 21 consecutive days.
- Female of non-child bearing potential, or female of child-bearing potential willing to use protocol-specified methods of contraception to prevent pregnancy during the study.
- Capable to comply with dosing of study drug, background AED, all study procedures and to maintain an accurate and complete daily written Seizure Calendar and Functional Status Diary

Exclusion Criteria:

- Have generalized epilepsy (e.g. Lennox-Gastaut, Juvenile Myoclonic epilepsy, Absence, etc.) or non-epileptic seizures.
- Have had innumerable seizures within the 12-month period prior to the Screening Visit where the individual seizures cannot be counted.
- Have had status epilepticus within 12 months prior to screening
- Have a history of pseudo seizures, non-epileptic events or any other type of psychogenic seizures that could be confused with seizures.
- Have been treated with felbamate or vigabatrin within the 6 months prior to Screening. If a subject has been previously treated with vigabatrin >6 months prior to Screening, a visual perimetry test performed within 6 months prior to Screening must show normal visual fields or no worsening of recognized visual field abnormalities as compared with prior to vigabatrin treatment
- Benzodiazepines used in any manner other than acute usage as defined in this protocol will be considered concurrent AED usage and will not be permitted
    - Are using Central Nervous System (CNS)-active medication (other than concomitant AED therapy), unless the subject has been stabilized on such medication for at least 1 month prior to the Screening Visit.
- Are using herbal treatments with CNS activity within at least 1 month prior to the Screening Visit
- Have received ezogabine/retigabine in a previous study or have taken POTIGA or TROBALT.
- Are currently following or planning to follow the ketogenic diet
- Have an active Vagus Nerve Stimulator (VNS) to control seizures
- Are planning surgery to control seizures during the study
- Have impaired renal function as judged by a creatinine clearance of <50 mL/min
- Have a history of urinary retention or risk factors for urinary retention that in the investigator's judgment could potentially affect subject safety.
- Have an average corrected QT interval (QTc), using Bazett's QT correction (QTcB), ≥450msec or ≥480msec for subjects with bundle branch block at the time of the Screening Visit
- Liver function tests: alanine aminotransferase (ALT) is ≥2 times the upper limit of normal (ULN); alkaline phosphatase and bilirubin are >1.5 × ULN (isolated bilirubin >1.5 × ULN is acceptable if bilirubin is fractionated and direct bilirubin is <35%).
- Are suffering from acute or progressive neurological disease, severe psychiatric disease, or severe mental abnormalities that are likely to interfere with the objectives of the study
- Have a history of malignancy within the past 2 years; with the exception of basal cell carcinoma
- Have unstable liver disease [chronic stable hepatitis B and C are acceptable if subject otherwise meets entry criteria; chronic stable Hepatitis B to be excluded if significant immunosuppressive agents administered due to risk of hepatitis B reactivation]
- Have any medical condition that, in the investigator's judgment, is considered to be clinically significant and could potentially affect subject safety or study outcome, including but not limited to: clinically significant cardiac, renal, hepatic condition, or a condition that affects the absorption, distribution, metabolism or excretion of drugs
- Have an active suicidal plan/intent or have had active suicidal thoughts in the past 6 months. Have history of suicide attempt in the last 2 years or more than 1 lifetime suicide attempt.
- Have a history of substance abuse (alcohol or drugs) or substance dependence within 12 months prior to screening
- Have a known hypersensitivity to any components of the study medication
- Have taken an investigational drug, or used an investigational device, within the previous 30 days prior to screening or plans to take an investigational drug

anytime during the study.

Contacts and Locations

Locations

United States, California

GSK Investigational Site

Fresno, California, United States, 93710

GSK Investigational Site

Newport Beach, California, United States, 92663

GSK Investigational Site

Newport Beach, California, United States, 92658

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GSK Investigational Site
San Antonio, Texas, United States, 78229
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Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	116878
Health Authority:	Romania: Agentia Nationala a Medicamentului

Poland: Urzad Rejestracji Produktow Leczniczych, Wyrobow Medycznych I Produktow Biobojczych
United States: Food and Drug Administration
Greece: National Drug Organisation

Study Results

Participant Flow

Recruitment Details

This was a randomized, double-blind, placebo-controlled, parallel-group, multicenter study comparing ezogabine/retigabine immediate release (IR) with placebo, as adjunctive treatment in adults with partial-onset seizures. The study was prematurely discontinued after randomizing only 6 of the planned 208 participants.

Pre-Assignment Details

The study consisted of a 2-week (or less) Screening Phase, an 8-week Baseline Phase, a 2-week Titration Phase, an 8-week Dose-Optimization Phase, an 8-week Maintenance Phase, and a 3-week Taper Phase.

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally three times a day (TID) in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 milligrams (mg)/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Overall Study

	Placebo	Ezogabine/Retigabine IR
Started	2	4
Completed	0	0
Not Completed	2	4
Study Closed / Terminated	2	2
Physician Decision	0	1
Withdrawal by Subject	0	1

Baseline Characteristics

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Baseline Measures

	Placebo	Ezogabine/Retigab IR	Total
Number of Participants	2	4	6
Age, Continuous [units: Years] Mean (Standard Deviation)	42.5 (10.61)	42.8 (16.32)	42.7 (13.50)

	Placebo	Ezogabine/Retigab IR	Total
Gender, Male/Female [units: Participants]			
Female	1	4	5
Male	1	0	1
Race/Ethnicity, Customized White - White/Caucasian/European [units: Participants]	2	4	6

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change in the 28-day Total Partial Seizure Frequency (POS) From Week 0 (End of Baseline Phase) Through Week 18 (End of Maintenance Phase)
Measure Description	The efficacy of ezogabine/retigabine IR as an adjunctive treatment was to be evaluated by the percent change in the total partial seizure frequency, which was recorded by participants in the daily seizure calendar. The total 28-day POS rate is defined as the total number of POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all randomized participants who received >= 1 dose of study medication and who had >= 1 post-Baseline seizure diary day with >= 0 seizures recorded.

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

2. Primary Outcome Measure:

Measure Title	Percent Change in the 28-day Total Partial Seizure Frequency (POS) Within Each Stratum From Week 0 (End of Baseline Phase) Through Week 18 (End of Maintenance Phase)
Measure Description	The percent change in 28-day total POS frequency within each stratum (sodium channel blocker or non-sodium channel blocker) background antiepileptic drug (AED) was to be summarized as the supportive analysis. The total 28-day POS value is defined as the total number of

	POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

3. Secondary Outcome Measure:

Measure Title	Percent Change in 28-day Total Partial Seizure Frequency (POS) for the Indicated Intervals: Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase
Measure Description	The efficacy of ezogabine/retigabine IR as an adjunctive treatment was to be evaluated by the percent change in total partial seizure frequency during the Dose-Optimization Phase and Maintenance Phase. The total 28-day POS value is defined as the total number of POS reported during the evaluation period divided by the total number of applicable days during the evaluation period with this quotient multiplied by 28 days. The applicable days are the days in which the participant had non-missing seizure data (i.e., either 0 or > 0 seizures recorded). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 3 (start of Dose -Optimization Phase) to Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

4. Secondary Outcome Measure:

Measure Title	Number of Par. Experiencing >=50% Reduction in 28-day Total Partial Seizure Frequency (POS) for the Intervals: Double-blind Period (Titration Phase + Dose-Optimization Phase + Maintenance Phase), Maintenance Phase and Dose-Optimization + Maintenance Phase
Measure Description	Participants (par.) experiencing >= 50% reduction from Baseline to the end of the Double-Blind Phase in 28-day total POS were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase) through Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.

	Description
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

5. Secondary Outcome Measure:

Measure Title	Number of Seizure Free Participants for the Indicated Intervals: Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase
Measure Description	Participants without seizures during the interval of Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 3 (start of Dose-Optimization Phase) to Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Number of Seizure Free Days for the Indicated Intervals: Double-blind Period (Titration Phase + Dose-Optimization Phase + Maintenance Phase), Maintenance Phase and the Dose-Optimization + Maintenance Phase
Measure Description	The change in number of seizure free days during the Double-Blind period, the Maintenance Phase and the Dose-Optimization Phase + Maintenance Phase were to be reported. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase) to Week 18 (end of Maintenance Phase)

Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

7. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Functional Status (Epilepsy-related Worry and Activity Limitation) and Productivity (Missed Work or School) to the End of the Dose-Optimization Phase and the End of the Maintenance Phase
Measure Description	The effect of ezogabine/retigabine IR as an adjunctive treatment on health outcomes was to be evaluated on the basis of functional status

	and productivity. Participants were asked to complete the paper functional status diary to collect information to assess how the participant's functional status is affected by their epilepsy symptoms. Participants were asked to rate their epilepsy-related worry, activity limitations, and productivity (missed work or school). Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 3 (start of Dose -Optimization Phase) to Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

8. Secondary Outcome Measure:

Measure Title	Incidence of New Seizure Types in Participants Without a History of These Seizure Types
Measure Description	The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the incidence of new seizure types in participants without a history of these seizure types. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase) to Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population: all randomized participants who receive >= 1 dose of study medication.

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

9. Secondary Outcome Measure:

Measure Title	Number of Participants at Each Dose During the Maintenance Phase and Average Maintenance Dose Over All Participants
Measure Description	The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the number of participants at each dose during the Maintenance Phase and the average maintenance dose over all participants. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 11 (start of Maintenance Phase) to Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

10. Secondary Outcome Measure:

Measure Title	Number of Participants With Early Study Discontinuation
Measure Description	The safety and tolerability of ezogabine/retigabine IR was to be evaluated by recording the incidence of participants with early study discontinuation.
Time Frame	Week 0 (end of Baseline Phase) to Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	2	4
Number of Participants With Early Study Discontinuation [units: Participants]	2	4

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in Body Weight
Measure Description	Change from Baseline in body weight was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

12. Secondary Outcome Measure:

Measure Title	Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)
Measure Description	Change from Baseline in blood pressure was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in Heart Rate
Measure Description	Change from Baseline in heart rate was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

14. Secondary Outcome Measure:

Measure Title	Change From Baseline in the QT Interval Using Bazett's Correction (QTcB) and QT Interval Using Fridericia's Correction (QTcF)
Measure Description	Change from Baseline in the QT interval using Bazett's correction (QTcB) and QT interval using Fridericia's correction were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day,

	Description
	750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

15. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Percentage of Basophils, Eosinophils, Lymphocytes, Monocytes, Neutrophils, Segmented Neutrophils and Red Blood Cell (RBC) Distribution Width
Measure Description	The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

16. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Basophils, Eosinophils, Lymphocytes, Monocytes, Neutrophils, Segmented Neutrophils, White Blood Cell (WBC) Count and Platelet Count
Measure Description	The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

17. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hemoglobin and Mean Corpuscle Hemoglobin Concentration
Measure Description	The change from Baseline in the indicated hematology tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)

Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

18. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hematocrit
Measure Description	The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)

Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

19. Secondary Outcome Measure:

Measure Title	Change From Baseline in Red Blood Cell (RBC) Count
Measure Description	The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)

Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

20. Secondary Outcome Measure:

Measure Title	Change From Baseline in Mean Corpuscle Hemoglobin
Measure Description	The change from Baseline in the indicated hematology test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)

Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

21. Secondary Outcome Measure:

Measure Title	Change From Baseline in Albumin and Total Protein
Measure Description	The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)

Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

22. Secondary Outcome Measure:

Measure Title	Change From Baseline in Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Creatine Kinase, Lactate Dehydrogenase and Gamma Glutamyltransferase (GGT)
Measure Description	The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.

Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

23. Secondary Outcome Measure:

Measure Title	Change From Baseline in Direct Bilirubin, Indirect Bilirubin, Total Bilirubin, Uric Acid and Creatinine
Measure Description	The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was

	not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

24. Secondary Outcome Measure:

Measure Title	Change From Baseline in Calcium, Chloride, Potassium, Sodium, Glucose, Magnesium, Phosphorus Inorganic,

	Bicarbonate and Urea/Blood Urea Nitrogen (BUN)
Measure Description	The change from Baseline in the indicated chemistry tests were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

25. Secondary Outcome Measure:

Measure Title	Change From Baseline in BUN/Creatinine Ratio
Measure Description	The change from Baseline in the indicated chemistry tests was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

26. Secondary Outcome Measure:

Measure Title	Change From Baseline in Creatinine Clearance
Measure Description	The change from Baseline in the indicated chemistry test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

27. Secondary Outcome Measure:

Measure Title	Change From Baseline in Urine Specific Gravity (USG)
Measure Description	The change from Baseline in the indicated urinalysis test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

28. Secondary Outcome Measure:

Measure Title	Change From Baseline in Urine Potential of Hydrogen (pH)
Measure Description	The change from Baseline in the indicated urinalysis test was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize ot evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

29. Secondary Outcome Measure:

Measure Title	Number of Participants for the Indicated Urinalysis Parameters Tested by Dipstick
Measure Description	The change from Baseline in the following urinalysis parameters (urine occult blood, urine glucose, urine ketones and urine protein) were to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Screening, Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase), Week 18 (end of Maintenance Phase) and Week 21 (end of Taper Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

30. Secondary Outcome Measure:

Measure Title	Change From Baseline in Post-void Residual (PVR) Urinary Bladder Ultrasound Volume
Measure Description	The change from Baseline in the PVR bladder ultrasound results was to be assessed. Due to the study being prematurely terminated, there was not sufficient data to summarize or evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase), Week 10 (end of Dose-Optimization Phase) and Week 18 (end of Maintenance Phase)
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

31. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Assessment Events of Suicidal Behavior, Suicidal Ideation or Non-suicidal Self Injurious Behavior Via the Columbia Suicide Severity Rating Scale (C-SSRS)
Measure Description	Prospective assessment of suicidality was conducted using the Columbia-Suicide Severity Rating Scale (C-SSRS), a brief questionnaire designed to assess severity and change in suicidality by integrating both behavior and ideation using a semi-structured interview to probe participant responses. C-SSRS data were only collected through Week 8 for the 6 randomized participants. Due to the study being prematurely terminated, there was not sufficient data to evaluate this endpoint.
Time Frame	Week 0 (end of Baseline Phase), Week 2 (end of Titration Phase), Week 4, Week 6 and Week 8
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in

	Description
	equally or unequally divided doses.

Measured Values

	Placebo	Ezogabine/Retigabine IR
Number of Participants Analyzed	2	4
Number of Participants With the Indicated Assessment Events of Suicidal Behavior, Suicidal Ideation or Non-suicidal Self Injurious Behavior Via the Columbia Suicide Severity Rating Scale (C-SSRS) [units: Participants]	0	0

Reported Adverse Events

Reporting Groups

	Description
Placebo	Participants received matching ezogabine/retigabine IR placebo orally TID in equally or unequally divided doses.
Ezogabine/Retigabine IR	Participants received investigator-selected daily doses of 600 mg/day, 750 mg/day, 900 mg/day, 1050 mg/day or 1200 mg/day of ezogabine/retigabine IR. The study drug was taken orally TID in equally or unequally divided doses.

Time Frame

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of the investigational product

until the Follow-up period (up to Study Day 147).

Additional Description

SAEs and non-serious AEs are reported for members of the Safety Population, comprised of all participants who received at least one dose of study treatment.

Serious Adverse Events

	Placebo	Ezogabine/Retigabine IR
Total # participants affected/at risk	0/2 (0%)	0/4 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Placebo	Ezogabine/Retigabine IR
Total # participants affected/at risk	1/2 (50%)	0/4 (0%)
Gastrointestinal disorders		
Toothache †[A]		
# participants affected/at risk	1/2 (50%)	0/4 (0%)
# events		
Musculoskeletal and connective tissue disorders		
Arthralgia †[A]		

	Placebo	Ezogabine/Retigabine IR
# participants affected/at risk	1/2 (50%)	0/4 (0%)
# events		
Nervous system disorders		
Somnolence †[A]		
# participants affected/at risk	1/2 (50%)	0/4 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: GSK Response Center
Organization: GlaxoSmithKline
Phone: 866-435-7343
Email: