Clinical trial results:
A Multicentre, Open-Label, Long-Term, Safety and Tolerability Study of Retigabine Immediate Release (IR) in Adults with Partial-Onset Seizures (Extension of Study RGB113905)

Summary

EudraCT number	2010-022777-34
Trial protocol	DE NL IT ES BG BE PL
Global end of trial date	13 September 2017

Results information

Result version number	v3 (current)
This version publication date	21 June 2018
First version publication date	22 December 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	113413

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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2016
Global end of trial reached?	Yes
Global end of trial date	13 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess long-term safety and tolerability of flexibly dosed retigabine immediate release (IR) as adjunctive therapy in adults with partial-onset seizures (POS) who completed open-label flexible dose Study RGB113905.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Russian Federation: 42
Country: Number of subjects enrolled	Thailand: 8
Country: Number of subjects enrolled	Ukraine: 16
Worldwide total number of subjects	98
EEA total number of subjects	32

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	94
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with partial-onset seizures (POS) who successfully completed the 20 weeks of treatment in parent study NCT01336621 were recruited in this open-label extension (OLE) study. The study was conducted in two periods, a primary treatment phase and a safety follow-up continuation phase (SFUCP).

Pre-assignment

Screening details:

Screening was performed on the same day as the final visit of the parent study NCT01336621. A total of 98 participants completed the parent study and opted to enter into this study. All participants received at least one dose of retigabine immediate release (IR) tablets.

Period 1

Period 1 title	Primary Reporting Phase (Upto 5.8 years)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Retigabine IR

Arm description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Arm type	Experimental
Investigational medicinal product name	Retigabine immediate release (IR)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Five strengths of retigabine IR including 50 mg, 100 mg, 200 mg, 300 mg and 400 mg tablets were provided. Participants entering RTG113413 from the parent study continued on the same maintenance dose of retigabine IR as per parent study. The dose was increased in steps of 50 mg to 150 mg/day on a weekly basis. The overall daily dose of retigabine IR was maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Number of subjects in period 1	Retigabine IR
Started	98
Completed	0
Not completed	98
Continued into SFUCP	9
Consent withdrawn by subject	27
Physician decision	2
Other: Reached stopping criteria	22

Adverse event, non-fatal	11
Other: study terminated	11
Other: lost to follow up	2
Lack of efficacy	2
Protocol deviation	12

Period 2

Period 2 title	SFUCP (Upto 2.6 years)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Retigabine IR

Arm description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Arm type	Experimental
Investigational medicinal product name	Retigabine immediate release (IR)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Five strengths of retigabine IR including 50 mg, 100 mg, 200 mg, 300 mg and 400 mg tablets were provided. Participants entering RTG113413 from the parent study continued on the same maintenance dose of retigabine IR as per parent study. The dose was increased in steps of 50 mg to 150 mg/day on a weekly basis. The overall daily dose of retigabine IR was maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Number of subjects in period 2	Retigabine IR
Started	9
Completed	0
Not completed	9
Study closed/terminated	3
Consent withdrawn by subject	3
Physician decision	1
Reached stopping criteria	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Retigabine IR

Reporting group description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Reporting group values	Retigabine IR	Total	
Number of subjects	98	98	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 39.2 ± 13.19	 -	
Gender categorical Units: Subjects			
Female Male	48 50	48 50	
Race/Ethnicity, Customized Units: Subjects			
Asian: South East Asian Heritage White- White/Caucasian/ European Heritage	8 90	8 90	

End points

End points reporting groups

Reporting group title	Retigabine IR

Reporting group description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Reporting group title	Retigabine IR

Reporting group description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Primary: Number of participants with treatment emergent adverse events (TEAEs) and serious AEs (TESAEs)

End point title	Number of participants with treatment emergent adverse events (TEAEs) and serious AEs (TESAEs)[1]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. 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, is a congenital anomaly/ birth defect or is associated with liver injury or impaired liver function. TEAE refers to an AE for which the onset was on or after the date of the first retigabine dose in this study and on or before 30 days after the last retigabine dose date. AEs that started in the parent study that increased in severity during this study were also considered treatment-emergent. The analysis was performed on Safety Population, which included participants who took at least one dose of study medication after they had enrolled into this OLE study.

End point type	Primary

End point timeframe:

Up to 5.8 years

Notes:

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

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[2]			
Units: Participants				
Any TEAE	38			
Any TESAE	4			

Notes:

[2] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with AEs and SAEs: All SFUCP subjects

End point title	Number of participants with AEs and SAEs: All SFUCP

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. 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, is a congenital anomaly/ birth defect or is associated with liver injury or impaired liver function. The following AEs were collected in the SFUCP: AEs related to the finding(s) of pigmentation/, discoloration of the eye /skin, AEs related to unexplained vision loss, SAEs, Deaths and Pregnancies. SFUCP collected AEs are those for which onset was 31 days or more after the last dose of retigabine. The analysis was performed on the All SFUCP Subjects population which comprised of all subjects who enter the SFUCP.

End point type	Primary

End point timeframe:

Up to 2.6 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	9[4]			
Units: Participants				
number (not applicable)				
Any AE	3			
Any SAE	1			

Notes:

[4] - All SFUCP subjects

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants withdrawn due to TEAEs

End point title	Number of participants withdrawn due to TEAEs[5]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolonged existing hospitalization, results in disability, is a congenital anomaly/birth defect or is associated with liver injury or impaired liver function. TEAE refers to an AE for which the onset was on or after the date of the first retigabine dose and on or before 30 days after the last retigabine dose date.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[6]			
Units: Participants				
Participants	16			

Notes:

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with retinal pigmentary abnormalities

End point title	Number of participants with retinal pigmentary abnormalities[7]

End point description:

Number of participants with abnormal findings after eye examination were evaluated. Only retinal pigmentary abnormalities detected on-treatment with retigabine were presented. Retinal pigmentary abnormalities included abnormalities in the macula, peripheral retina and unspecified location. Only those participants with >=1 ophthalmology exam on or before last dose of RTG are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	53[8]			
Units: Participants				
Participants	8			

Notes:

[8] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with pigmentation of non-retinal ocular tissue(s)

End point title	Number of participants with pigmentation of non-retinal ocular tissue(s)[9]

End point description:

Number of participants with abnormal findings after eye examination were evaluated. Pigmentation of non-retinal ocular tissue (s) detected on-treatment with retigabine were presented. Non-retinal pigmentary abnormalities included abnormalities in the sclera and/ or conjunctiva, cornea, iris and lens. Only those participants with >=1 ophthalmology exam on or before last dose of RTG are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	53[10]			
Units: Participants				
Participants	15			

Notes:

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal discoloration of skin

End point title	Number of participants with abnormal discoloration of skin[11]

End point description:

Number of participants with Dermatologist-Confirmed abnormal discoloration of skin including skin around the eyes and eyelids, lips, nails, or mucosa were evaluated. Only abnormalities occurring on-treatment with retigabine were presented. Only those participants who had at least one skin exam by the investigator or dermatologist on or before the last dose of RTG or dermatologist-confirmed discoloration with start date on or before the date of last dose of RTG are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	58[12]			
Units: Participants				
Any abnormal discoloration	11			
Discoloration of skin	5			
Discoloration of lips	3			
Discoloration of nails	10			
Discoloration of mucosa	9			

Notes:

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with a clinically significant decrease in visual acuity from initial examination

End point title	Number of participants with a clinically significant decrease in

	visual acuity from initial examination[13]

End point description:

Number of participants with a clinically significant decrease in visual acuity from initial examination were evaluated. Only abnormalities occurring on-treatment with retigabine were presented. Only those participants with both initial and at least 1 follow-up exam while on RTG treatment are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	48[14]			
Units: Participants				
Participants	3			

Notes:

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with decrease in confrontational visual field from initial examination

End point title	Number of participants with decrease in confrontational visual field from initial examination[15]

End point description:

Number of participants with a clinically significant decrease in confrontational visual field from initial examination were evaluated. Only abnormalities occurring on-treatment with retigabine were presented. Only those subjects with both initial and at least 1 follow-up exam while on RTG treatment are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	48[16]			
Units: Participants				
Participants	1			

Notes:

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with potential clinical concern (PCC) values of change from Baseline in vital signs and weight

End point title	Number of participants with potential clinical concern (PCC) values of change from Baseline in vital signs and weight[17]

End point description:

Vital signs including systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were measured after at least 5 minutes of rest. Body weight was measured without shoes and wearing light clothing. Baseline assessments in this OLE study were defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was calculated by subtracting the Baseline value from the post-baseline value. Increase or decrease of >=20 in SBP, increase or decrease of >=15 in DBP and HR were considered as PCC values. Number of participants with PCC values of vital signs for any visit post-Baseline are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[18]			
Units: Participants				
DBP; decrease of >=15	15			
DBP; increase of >=15	7			
HR; decrease of >=15	15			
HR; increase of >=15	18			
SBP; decrease of >=20	18			
SBP; increase of >=20	8			
Weight; decrease of >=7 percent	10			
Weight; increase of >=7 percent	32			

Notes:

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in electrocardiogram (ECG) parameter including HR

End point title	Change from Baseline in electrocardiogram (ECG) parameter including HR[19]

End point description:

Single measurements of 12-lead ECG were obtained in supine position after at least 10 minutes of rest using an ECG machine to measure HR. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[20]			
Units: Beats per minute (bpm)				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 89	-2.2 (± 10.54)			
Visit 2 (Week 13); n= 90	-0.6 (± 9.77)			
Visit 3 (Week 26); n= 80	-1.5 (± 9.21)			
Visit 4 (Week 39); n= 71	-1.7 (± 8.72)			
Visit 5 (Week 52); n= 67	-0.6 (± 10.30)			
Visit 6 (Week 69); n= 63	-0.2 (± 9.96)			
Visit 7 (Week 86); n= 56	1.6 (± 8.89)			
Visit 8 (Week 104); n= 42	-1.8 (± 10.30)			
Visit 9 (Week 121); n= 38	1.7 (± 11.01)			
Visit 10 (Week 138); n= 37	1.6 (± 12.17)			
Visit 11 (Week 156); n= 30	1.1 (± 10.23)			
Visit 12 (Week 173); n= 24	-0.8 (± 13.43)			
Visit 13 (Week 190); n= 19	2.7 (± 11.29)			
Visit 14 (Week 208); n= 10	5.6 (± 10.41)			
Visit 15 (Week 225); n= 5	-0.2 (± 8.04)			
Visit 16 (Week 242); n= 4	-4.3 (± 13.30)			
Visit 17 (Week 260); n= 4	-7.3 (± 6.95)			
Visit 18 (Week 277); n= 2	2.5 (± 9.19)			
Withdrawal visit; n= 83	-1.8 (± 11.49)			
Follow up visit; n= 59	-1.1 (± 11.95)			

Notes:

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in ECG parameter including PR interval, QRS duration, uncorrected QT interval, corrected QT by Bazett's formula (QTcB), corrected QT by Fridericia's formula (QTcF) and RR interval

End point title	Change from Baseline in ECG parameter including PR interval, QRS duration, uncorrected QT interval, corrected QT by Bazett's formula (QTcB), corrected QT by Fridericia's formula (QTcF) and RR interval[21]

End point description:

Single measurements of 12-lead ECG were obtained in supine position after at least 10 minutes of rest using an ECG machine to measure parameters including PR interval, QRS duration, uncorrected QT interval, QTcB, QTcF and RR interval. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[22]			
Units: Milliseconds (msec)				
arithmetic mean (standard deviation)				
PR interval; Visit 1 (Screening); n= 86	2.4 (± 13.11)			
PR interval; Visit 2 (Week 13); n= 88	1.3 (± 15.42)			
PR interval; Visit 3 (Week 26); n= 78	3.2 (± 12.99)			
PR interval; Visit 4 (Week 39); n= 70	1.2 (± 13.25)			
PR interval; visit 5 (Week 52); n= 66	-0.2 (± 13.17)			
PR interval; Visit 6 (Week 69); n= 62	1.3 (± 13.93)			
PR interval; Visit 7 (Week 86); n= 54	-0.7 (± 12.58)			
PR interval; Visit 8 (Week 104); n= 42	3.1 (± 10.85)			
PR interval; Visit 9 (Week 121); n= 38	-1.1 (± 12.79)			
PR interval; Visit 10 (Week 138); n= 37	1.2 (± 15.13)			
PR interval; Visit 11 (Week 156); n= 30	-0.5 (± 13.50)			
PR interval; Visit 12 (Week 173); n= 24	4.8 (± 11.89)			
PR interval; Visit 13 (week 190); n= 19	-2.1 (± 10.19)			
PR interval; Visit 14 (Week 208); n= 10	7.8 (± 15.03)			
PR interval; Visit 15 (Week 225); n= 5	8.4 (± 7.23)			
PR interval; Visit 16 (Week 242); n= 4	-3.0 (± 8.04)			
PR interval; Visit 17 (Week 260); n= 4	9.3 (± 11.09)			
PR interval; Visit 18 (Week 277); n= 2	-5.5 (± 7.78)			
PR interval; Withdrawal visit; n= 81	3.6 (± 13.86)			
PR interval; follow up visit; n= 57	3.7 (± 12.43)			
QRS duration; Visit 1 (Screening); n= 88	-0.1 (± 6.37)			
QRS duration; Visit 2 (Week 13); n= 89	0.2 (± 6.99)			
QRS duration; Visit 3 (Week 26); n= 80	1.1 (± 8.77)			
QRS duration; Visit 4 (Week 39); n= 71	1.1 (± 7.10)			
QRS duration; Visit 5 (Week 52); n= 67	0.9 (± 9.81)			
QRS duration; Visit 6 (Week 69); n= 63	1.9 (± 8.56)			
QRS duration; Visit 7 (Week 86); n= 55	-0.4 (± 7.20)			
QRS duration; Visit 8 (Week 104); n= 42	0.1 (± 6.40)			
QRS duration; Visit 9 (Week 121); n= 38	-0.7 (± 7.79)			
QRS duration; Visit 10 (Week 138); n= 37	-2.0 (± 7.85)			
QRS duration; Visit 11 (Week 156); n= 30	-3.3 (± 9.54)			
QRS duration; Visit 12 (Week 173); n= 24	-1.3 (± 9.04)			
QRS duration; Visit 13 (Week 190); n= 19	-4.9 (± 8.80)			
QRS duration; Visit 14 (Week 208); n= 10	-6.1 (± 6.34)			
QRS duration; Visit 15 (Week 225); n= 5	-2.9 (± 3.44)			

QRS duration; Visit 16 (Week 242); n= 4	-5.9 (± 9.58)			
QRS duration; Visit 17 (Week 260); n= 4	-7.8 (± 5.19)			
QRS duration; Visit 18 (Week 277); n= 2	-4.5 (± 2.12)			
QRS duration; withdrawal visit; n= 82	-2.5 (± 9.49)			
QRS duration; follow up visit; n= 59	0.0 (± 11.90)			
Uncorrected QT interval;Visit 1 (Screening); n= 85	10.1 (± 26.19)			
Uncorrected QT interval; Visit 2 (Week 13); n= 88	4.9 (± 23.43)			
Uncorrected QT interval; Visit 3 (Week 26); n= 78	7.9 (± 23.44)			
Uncorrected QT interval; Visit 4 (Week 39); n= 69	9.3 (± 23.77)			
Uncorrected QT interval; Visit 5 (Week 52); n= 65	6.6 (± 25.18)			
Uncorrected QT interval; Visit 6 (Week 69); n= 61	7.4 (± 26.39)			
Uncorrected QT interval; Visit 7 (Week 86); n= 53	-1.6 (± 23.81)			
Uncorrected QT interval; Visit 8 (Week 104); n= 41	6.0 (± 26.77)			
Uncorrected QT interval; Visit 9 (Week 121); n= 37	-0.5 (± 24.52)			
Uncorrected QT interval; Visit 10 (Week 138);n= 36	-8.7 (± 33.60)			
Uncorrected QT interval; Visit 11 (Week 156);n= 29	-4.9 (± 33.01)			
Uncorrected QT interval; Visit 12 (Week 173);n= 23	4.7 (± 25.06)			
Uncorrected QT interval; Visit 13 (Week 190);n= 19	-1.9 (± 26.01)			
Uncorrected QT interval; Visit 14 (Week 208);n= 10	-17.0 (± 27.93)			
Uncorrected QT interval; Visit 15 (Week 225);n= 5	-1.5 (± 5.68)			
Uncorrected QT interval; Visit 16 (Week 242);n= 4	3.1 (± 26.90)			
Uncorrected QT interval; Visit 17 (Week 260);n= 4	17.5 (± 36.08)			
Uncorrected QT interval; Visit 18 (Week 277);n= 2	-3.5 (± 36.06)			
Uncorrected QT interval; withdrawal visit; n= 80	5.2 (± 29.01)			
Uncorrected QT interval; follow up visit; n= 56	2.7 (± 28.41)			
QTcB; Visit 1 (Screening); n= 85	5.0 (± 17.35)			
QTcB; Visit 2 (Week 13); n= 88	3.2 (± 18.52)			
QTcB; Visit 3 (Week 26); n= 78	4.0 (± 16.48)			
QTcB; Visit 4 (Week 39); n= 69	6.0 (± 17.27)			
QTcB; Visit 5 (Week 52); n= 65	5.8 (± 17.14)			
QTcB; Visit 6 (Week 69); n= 61	6.8 (± 15.01)			
QTcB; Visit 7 (Week 86); n= 53	4.3 (± 15.71)			
QTcB; Visit 8 (Week 104); n= 41	2.5 (± 20.70)			
QTcB; Visit 9 (Week 121); n= 37	4.9 (± 16.01)			
QTcB; Visit 10 (Week 138); n= 36	-2.8 (± 16.46)			
QTcB; Visit 11 (Week 156); n= 29	-0.3 (± 19.63)			

QTcB; Visit 12 (Week 173); n= 23	4.2 (± 24.12)			
QTcB; Visit 13 (Week 190); n= 19	3.9 (± 20.16)			
QTcB; Visit 14 (Week 208); n= 10	-1.6 (± 14.91)			
QTcB; Visit 15 (Week 225); n= 5	-1.9 (± 18.26)			
QTcB; Visit 16 (Week 242); n= 4	-9.8 (± 15.09)			
QTcB; Visit 17 (Week 260); n= 4	-2.0 (± 27.12)			
QTcB; Visit 18 (Week 277); n= 2	4.5 (± 17.68)			
QTcB; withdrawal visit; n= 80	-0.7 (± 20.78)			
QTcB; follow up visit; n= 56	-1.0 (± 17.84)			
QTcF; Visit 1 (Screening); n= 85	6.8 (± 16.11)			
QTcF; Visit 2 (Week 13); n= 88	3.7 (± 15.74)			
QTcF; Visit 3 (Week 26); n= 78	5.4 (± 15.01)			
QTcF; Visit 4 (Week 39); n= 69	7.1 (± 16.58)			
QTcF; Visit 5 (Week 52); n= 65	6.1 (± 14.92)			
QTcF; Visit 6 (Week 69); n= 61	7.1 (± 14.47)			
QTcF; Visit 7 (Week 86); n= 53	2.3 (± 16.04)			
QTcF; Visit 8 (Week 104); n= 41	3.7 (± 19.31)			
QTcF; Visit 9 (Week 121); n= 37	3.0 (± 12.90)			
QTcF; Visit 10 (Week 138); n= 36	-4.8 (± 18.22)			
QTcF; Visit 11 (Week 156); n= 29	-1.8 (± 21.86)			
QTcF; Visit 12 (Week 173); n= 23	4.6 (± 17.51)			
QTcF; Visit 13 (Week 190); n= 19	1.9 (± 17.47)			
QTcF; Visit 14 (Week 208); n= 10	-7.0 (± 14.99)			
QTcF; Visit 15 (Week 225); n= 5	-1.6 (± 10.53)			
QTcF; Visit 16 (Week 242); n= 4	-5.4 (± 8.96)			
QTcF; Visit 17 (Week 260); n= 4	5.3 (± 29.75)			
QTcF; Visit 18 (Week 277); n= 2	2.0 (± 24.04)			
QTcF; withdrawal visit; n= 80	1.3 (± 18.24)			
QTcF; follow up visit; n= 56	0.3 (± 15.49)			
RR interval; visit 1 (Screening); n= 89	27.9 (± 120.57)			
RR interval; visit 2 (Week 13); n= 90	12.2 (± 115.82)			
RR interval; visit 3 (Week 26); n= 80	20.5 (± 110.48)			
RR interval; visit 4 (Week 39); n= 71	22.4 (± 107.77)			
RR interval; visit 5 (Week 52); n= 67	10.3 (± 128.05)			
RR interval; visit 6 (Week 69); n= 63	6.2 (± 127.01)			
RR interval; visit 7 (Week 86); n= 56	-18.5 (± 102.45)			
RR interval; visit 8 (Week 104); n= 42	23.7 (± 121.17)			
RR interval; visit 9 (Week 121); n= 38	-17.5 (± 134.18)			
RR interval; visit 10 (Week 138); n= 37	-19.6 (± 145.64)			
RR interval; visit 11 (Week 156); n= 30	-16.0 (± 120.50)			
RR interval; visit 12 (Week 173); n= 24	12.9 (± 163.66)			
RR interval; visit 13 (Week 190); n= 19	-19.5 (± 138.03)			
RR interval; visit 14 (Week 208); n= 10	-70.7 (± 130.51)			

RR interval; visit 15 (Week 225); n= 5	-2.8 (± 108.30)			
RR interval; visit 16 (Week 242); n= 4	56.6 (± 165.75)			
RR interval; visit 17 (Week 260); n= 4	83.5 (± 91.72)			
RR interval; visit 18 (Week 277); n= 2	-30.0 (± 86.27)			
RR interval; withdrawal visit; n= 83	29.1 (± 152.19)			
RR interval; follow up visit; n= 59	15.9 (± 150.13)			

Notes:

[22] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinical chemistry parameters of PCC

End point title	Number of participants with clinical chemistry parameters of PCC[23]

End point description:

Number of participants with chemistry parameters of PCC at 'any visit post-Baseline' are presented. Chemistry parameters for which PCC values were identified were alanine aminotransferase (ALT) (if value >=3 * upper limit of normal [ULN]), alkaline phosphatase (alk.phosphatase) (if value >=3*ULN), aspartate aminotransferase (AST) (if value >=3*ULN), calcium (if value <=1.8962 or >=2.8692), carbon-di-oxide (CO2) (if value <=18 or >=36), chloride (if value <=92 or >=112), creatine kinase (if value >=3*ULN), direct bilirubin (if value >=1.5*ULN), glucose (if value <=2.7755 or >=11.102), lactate dehydrogenase (LD) (if value >=3*ULN), magnesium (if value <0.36 or >2.50), potassium (if value <=3.0 or >=6.0), sodium (if value <=127 or >=153), total bilirubin (if value >=1.5*ULN), total protein (if value <45 or >100), blood urea nitrogen (BUN) (if value >=14.28). Only those participants with data available at specific time points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[24]			
Units: Participants				
ALT; high; n= 98	2			
Alk.phosphatase; high; n= 98	0			
AST; high; n= 98	1			
Calcium; high; n= 98	0			
Calcium; low; n= 98	0			
CO2 content/bicarbonate; high; n= 98	0			
CO2 content/bicrbonate; low; n= 98	10			
Chloride; high; n= 98	6			
Chloride; low; n= 98	2			
Creatine kinase; high; n= 98	6			
Creatinine; high; n= 98	0			
Direct bilirubin; high; n= 98	0			

Glucose; high; n= 98	3			
Glucose; low; n= 98	1			
LD ; high; n= 98	1			
Magnesium; high; n= 98	0			
Magnesium; low; n= 98	0			
Potassium; high; n= 98	1			
Potassium; low; n= 98	0			
Sodium; high; n= 91	0			
Sodium; low; n= 91	2			
Total bilirubin; high; n= 98	1			
Total protein; high; n= 98	0			
Total protein; low; n= 98	0			
BUN; high; n= 91	0			

Notes:

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with hematology parameters of PCC

End point title	Number of participants with hematology parameters of PCC[25]

End point description:

Blood samples were collected from participants to evaluate hematology parameters. Number of participants with clinical hematology parameters of PCC at 'any visit post-Baseline' are presented. Hematology parameters for which PCC values were identified were eosinophils (if value is >0.8), hematocrit (if value is <=0.32 for males and <=0.28 for females), platelet count (if value is <=100 or >=550), total neutrophils (if value is <=1.8), white blood cells (WBC) (if value is <=2.8 or >=16). Only those participants with data available at specific time points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[26]			
Units: Participants				
Eosinophils; high; n= 98	7			
Hematocrit; low; n= 98	4			
Hemoglobin; low; n= 98	3			
Platelet count; high; n= 98	1			
Platelet count; low; n= 98	4			
Total neutrophils; low; n= 98	20			
WBC; high; n= 91	2			
WBC; low; n= 91	3			

Notes:
[26] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with urinalysis parameters of PCC

End point title	Number of participants with urinalysis parameters of PCC[27]

End point description:

Urine samples were collected from participants at specific time points. Number of participants with urinalysis parameters of PCC at 'any visit post-Baseline' are presented. Urinalysis parameters for which PCC values were identified were albumin/creatinine ratio (if value is >11.3), red blood cells (RBC) (if value is 3-5 or higher), WBC (if value is 5-10 or higher for male and 10-15 or higher for females), specific gravity (if value is <1.001 or >1.035) and potential of hydrogen (pH) (if value is <4.6 or >8.0). Only those participants with data available at specific time points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[28]			
Units: Participants				
Albumin/creatinine ratio; high; n= 96	4			
RBC; high; n= 98	54			
WBC; high; n= 91	59			
Specific gravity; high; n= 91	4			
Specific gravity; low; n= 91	0			
pH; high; n= 98	1			
pH; low; n= 98	0			

Notes:
[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in albumin and total protein

End point title	Change from Baseline in albumin and total protein[29]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical chemistry parameters including albumin and total protein. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified

data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[30]			
Units: Gram per liter (G/L)				
arithmetic mean (standard deviation)				
Albumin; visit 1 (Screening); n= 83	-1.6 (± 2.72)			
Albumin; visit 2 (Week 13); n= 87	-0.9 (± 2.70)			
Albumin; visit 3 (Week 26); n= 75	-0.8 (± 2.83)			
Albumin; visit 4 (Week 39); n= 70	-0.7 (± 3.09)			
Albumin; visit 5 (Week 52); n= 65	-1.5 (± 3.25)			
Albumin; visit 6 (Week 69); n= 62	-1.1 (± 3.11)			
Albumin; visit 7 (Week 86); n= 54	-1.0 (± 2.70)			
Albumin; visit 8 (Week 104); n= 42	-1.6 (± 3.05)			
Albumin; visit 9 (Week 121); n= 39	-2.1 (± 2.88)			
Albumin; visit 10 (Week 138); n= 36	-2.2 (± 3.16)			
Albumin; visit 11 (Week 156); n= 30	-3.0 (± 3.62)			
Albumin; visit 12 (Week 173); n= 23	-1.7 (± 2.82)			
Albumin; visit 13 (Week 190); n= 19	-2.9 (± 3.62)			
Albumin; visit14 (Week 208); n= 10	-3.9 (± 3.78)			
Albumin; visit 15 (Week 225); n= 5	-3.4 (± 1.52)			
Albumin; visit 16 (Week242); n= 4	-4.3 (± 1.26)			
Albumin; visit 17 (Week 260); n= 4	-4.0 (± 1.15)			
Albumin; visit 18 (Week 277); n= 2	-4.5 (± 0.71)			
Albumin; withdrawal visit; n= 79	-1.8 (± 3.11)			
Albumin; follow up visit; n= 60	-2.3 (± 3.42)			
Total protein; visit 1 (Screening); n= 83	-2.0 (± 4.57)			
Total protein; visit 2 (Week 13); n= 87	-1.0 (± 4.59)			
Total protein; visit 3 (Week 26); n= 75	-1.5 (± 5.15)			
Total protein; visit 4 (Week 39); n= 70	-1.8 (± 4.13)			
Total protein; visit 5 (Week 52); n= 65	-2.6 (± 4.74)			
Total protein; visit 6 (Week 69); n= 62	-1.4 (± 4.09)			
Total protein; visit 7 (Week 86); n= 54	-1.0 (± 4.44)			
Total protein; visit 8 (Week 104); n= 42	-1.5 (± 4.65)			
Total protein; visit 9 (Week 121); n= 39	-2.1 (± 4.58)			
Total protein; visit 10 (Week 138); n= 36	-2.7 (± 4.90)			
Total protein; visit 11 (Week 156); n= 30	-3.2 (± 5.40)			
Total protein; visit 12 (Week 173); n= 23	-1.1 (± 4.07)			
Total protein; visit 13 (Week 190); n= 19	-1.9 (± 5.57)			
Total protein; visit 14 (Week 208); n= 10	-3.1 (± 3.41)			

Total protein; visit 15 (Week 225); n= 5	-3.4 (± 2.51)			
Total protein; visit 16 (Week 242); n= 4	-3.8 (± 4.99)			
Total protein; visit 17 (Week 260); n= 4	-2.3 (± 3.30)			
Total protein; visit 18 (Week 277); n= 2	-4.5 (± 2.12)			
Total protein; withdrawal visit; n= 79	-2.5 (± 5.27)			
Total protein; follow up visit; n= 60	-2.1 (± 6.12)			

Notes:

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in alk. phosphatase, ALT, AST, creatine kinase and LD levels

End point title	Change from Baseline in alk. phosphatase, ALT, AST, creatine kinase and LD levels[31]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical chemistry parameters including alk. phosphatase, ALT, AST, creatine kinase and LD. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[32]			
Units: International unit per liter (IU/L)				
arithmetic mean (standard deviation)				
Alk. phosphatase; visit 1 (Screening); n= 82	-2.7 (± 15.51)			
Alk. phosphatase; visit 2 (Week 13); n= 86	1.1 (± 14.02)			
Alk. phosphatase; visit 3 (Week 26); n= 75	3.5 (± 15.80)			
Alk. phosphatase; visit 4 (week 39); n= 70	3.9 (± 15.46)			
Alk. phosphatase; visit 5 (Week 52); n= 65	1.0 (± 15.36)			
Alk. phosphatase; visit 6 (Week 69); n= 62	4.1 (± 14.22)			
Alk. phosphatase; visit 7 (Week 86); n= 54	4.0 (± 16.01)			
Alk. phosphatase; visit 8 (Week 104); n= 42	-0.3 (± 18.27)			
Alk. phosphatase; visit 9 (Week 121); n= 39	2.4 (± 16.33)			
Alk. phosphatase; visit 10 (Week 138); n= 36	2.2 (± 21.08)			

Alk. phosphatase; visit 11 (Week 156); n= 30	-1.4 (± 18.49)			
Alk. phosphatase; visit 12 (Week 173); n= 23	5.5 (± 20.76)			
Alk. phosphatase; visit 13 (Week 190); n= 19	6.3 (± 23.61)			
Alk. phosphatase; visit 14 (Week 208); n= 10	6.1 (± 19.84)			
Alk. phosphatase; visit 15 (Week 225); n= 5	5.8 (± 16.95)			
Alk. phosphatase; visit 16 (Week 242); n= 4	9.5 (± 15.55)			
Alk. phosphatase; visit 17 (Week 260); n= 4	7.3 (± 7.14)			
Alk. phosphatase; visit 18 (Week 277); n= 2	-4.5 (± 10.61)			
Alk. phosphatase; withdrawal visit; n= 78	2.5 (± 19.86)			
Alk. phosphatase; follow up visit; n= 60	-0.3 (± 19.59)			
ALT; visit 1 (Screening); n= 83	1.3 (± 10.90)			
ALT; visit 2 (Week 13); n= 87	3.4 (± 23.41)			
ALT; visit 3 (Week 26); n= 76	1.0 (± 23.35)			
ALT; visit 4 (Week 39); n= 70	-0.5 (± 10.22)			
ALT; visit 5 (Week 52); n= 65	-0.4 (± 8.21)			
ALT; visit 6 (Week 69); n= 62	0.0 (± 11.51)			
ALT; visit 7 (Week 86); n= 54	-1.9 (± 10.02)			
ALT; visit 8 (Week 104); n= 42	-1.5 (± 8.58)			
ALT; visit 9 (Week 121); n= 39	0.4 (± 8.80)			
ALT; visit 10 (Week 138); n= 36	3.4 (± 21.74)			
ALT; visit 11 (Week 156); n= 29	-1.1 (± 8.21)			
ALT; visit 12 (Week 173); n= 23	-1.3 (± 7.97)			
ALT; visit 13 (Week 190); n= 19	0.0 (± 8.10)			
ALT; visit 14 (Week 208); n= 10	0.7 (± 7.32)			
ALT; visit 15 (Week 225); n= 5	-2.0 (± 4.47)			
ALT; visit 16 (Week 242); n= 4	-0.5 (± 8.54)			
ALT; visit 17 (Week 260); n= 4	0.0 (± 6.98)			
ALT; visit 18 (Week 277); n= 2	3.5 (± 3.54)			
ALT; withdrawal visit; n= 79	0.7 (± 10.17)			
ALT; follow up visit; n= 60	0.1 (± 8.43)			
AST; visit 1 (Screening); n= 82	1.7 (± 7.97)			
AST; visit 2 (Week 13); n= 86	5.1 (± 31.13)			
AST; visit 3 (Week 26); n= 75	2.9 (± 23.95)			
AST; visit 4 (Week 39); n= 70	1.3 (± 8.23)			
AST; visit 5 (Week 52); n= 65	2.5 (± 6.01)			
AST; visit 6 (Week 69); n= 62	1.5 (± 7.55)			
AST; visit 7 (Week 86); n= 54	1.7 (± 8.20)			
AST; visit 8 (Week 104); n= 42	1.5 (± 7.94)			
AST; visit 9 (Week 121); n= 39	2.6 (± 7.99)			
AST; visit 10 (Week 138); n= 36	6.4 (± 17.36)			
AST; visit 11 (Week 156); n= 30	1.4 (± 7.38)			
AST; visit 12 (Week 173); n= 23	2.7 (± 4.71)			
AST; visit 13 (Week 190); n= 19	3.3 (± 5.21)			
AST; visit 14 (Week 208); n= 10	3.5 (± 6.42)			
AST; visit 15 (Week 225); n= 5	4.2 (± 2.95)			
AST; visit 16 (Week 242); n= 4	4.3 (± 4.72)			

AST; visit 17 (Week 260); n= 4	5.5 (± 3.11)			
AST; visit 18 (Week 277); n= 2	10.0 (± 9.90)			
AST; withdrawal visit; n= 78	1.8 (± 7.87)			
AST; follow up visit; n= 60	1.2 (± 6.99)			
Creatine kinase; Visit 1 (Screening); n= 82	16.4 (± 132.76)			
Creatine kinase; Visit 2 (Week 13); n= 86	11.3 (± 78.18)			
Creatine kinase; Visit 3 (Week 26); n= 74	11.7 (± 59.78)			
Creatine kinase; Visit 4 (Week 39); n= 70	49.4 (± 397.67)			
Creatine kinase; Visit 5 (Week 52); n= 65	31.3 (± 136.41)			
Creatine kinase; Visit 6 (Week 69); n= 62	11.1 (± 55.13)			
Creatine kinase; Visit 7 (Week 86); n= 54	23.6 (± 92.64)			
Creatine kinase; Visit 8 (Week 104); n= 42	33.2 (± 110.99)			
Creatine kinase; Visit 9 (Week 121); n= 39	22.5 (± 77.04)			
Creatine kinase; Visit 10 (Week 138); n= 36	24.8 (± 83.80)			
Creatine kinase; Visit 11 (Week 156); n= 30	31.9 (± 86.68)			
Creatine kinase; Visit 12 (Week 173); n= 23	29.1 (± 97.10)			
Creatine kinase; Visit 13 (Week 190); n= 19	50.2 (± 125.12)			
Creatine kinase; Visit 14 (Week 208); n= 10	-7.9 (± 101.39)			
Creatine kinase; Visit 15 (Week 225); n= 5	42.6 (± 99.09)			
Creatine kinase; Visit 16 (Week 242); n= 4	90.3 (± 127.49)			
Creatine kinase; Visit 17 (Week 260); n= 4	78.8 (± 110.78)			
Creatine kinase; Visit 18 (Week 277); n= 2	-27.5 (± 102.53)			
Creatine kinase; withdrawal visit; n= 78	28.7 (± 139.96)			
Creatine kinase; follow up visit; n= 60	33.9 (± 128.19)			
LD; visit 1(Screening); n= 82	3.7 (± 23.16)			
LD; visit 2 (Week 13); n= 86	4.3 (± 32.66)			
LD; visit 3 (Week 26); n= 74	0.0 (± 27.88)			
LD; visit 4 (Week 39); n= 69	0.4 (± 28.51)			
LD; visit 5 (Week 52); n= 64	2.1 (± 28.01)			
LD; visit 6 (Week 69); n= 61	-0.1 (± 25.98)			
LD; visit 7 (Week 86); n= 54	9.2 (± 30.42)			
LD; visit 8 (Week 104); n= 42	4.7 (± 29.37)			
LD; visit 9 (Week 121); n= 39	18.8 (± 53.56)			
LD; visit 10 (Week 138); n= 36	33.0 (± 131.87)			
LD; visit 11 (Week 156); n= 30	13.7 (± 33.18)			
LD; visit 12 (Week 173); n= 23	4.1 (± 31.91)			
LD; visit 13 (Week 190); n= 19	30.0 (± 58.17)			
LD; visit 14 (Week 208); n= 10	25.8 (± 42.76)			

LD; visit 15 (Week 225); n= 5	34.6 (± 25.93)			
LD; visit 16 (Week 242); n= 4	25.8 (± 15.97)			
LD; visit 17 (Week 260); n= 4	20.8 (± 25.86)			
LD; visit 18 (Week 277); n= 2	52.0 (± 60.81)			
LD; withdrawal visit; n= 78	7.8 (± 31.17)			
LD; follow up visit; n= 60	5.6 (± 36.94)			

Notes:

[32] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in direct bilirubin, total bilirubin and creatinine

End point title	Change from Baseline in direct bilirubin, total bilirubin and creatinine[33]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical chemistry parameters including direct bilirubin, total bilirubin and creatinine. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[34]			
Units: Micromole per liter (µmol/L)				
arithmetic mean (standard deviation)				
Direct bilirubin; visit 1 (Screening); n= 83	0.1 (± 0.95)			
Direct bilirubin; visit 2 (Week 13); n= 87	-0.1 (± 0.96)			
Direct bilirubin; visit 3 (Week 26); n= 75	-0.2 (± 0.94)			
Direct bilirubin; visit 4 (Week 39); n= 69	-0.1 (± 0.91)			
Direct bilirubin; visit 5 (Week 52); n= 65	0.0 (± 0.95)			
Direct bilirubin; visit 6 (Week 69); n= 62	0.0 (± 0.97)			
Direct bilirubin; visit 7 (Week 86); n= 54	-0.2 (± 1.17)			
Direct bilirubin; visit 8 (Week 104); n= 42	0.0 (± 0.91)			
Direct bilirubin; visit 9 (Week 121); n= 39	-0.2 (± 0.87)			
Direct bilirubin; visit 10 (Week 138); n= 36	-0.1 (± 1.27)			

Direct bilirubin; visit 11 (Week 156); n= 30	0.0 (± 0.72)			
Direct bilirubin; visit 12 (Week 173); n= 23	-0.1 (± 0.73)			
Direct bilirubin; visit 13 (Week 190); n= 19	0.1 (± 0.91)			
Direct bilirubin; visit 14 (Week 208); n= 10	0.0 (± 0.67)			
Direct bilirubin; visit 15 (Week 225); n= 5	-0.2 (± 0.84)			
Direct bilirubin; visit 16 (Week 242); n= 4	-0.5 (± 1.00)			
Direct bilirubin; visit 17 (Week 260); n= 4	-0.5 (± 1.29)			
Direct bilirubin; visit 18 (Week 277); n= 2	0.5 (± 2.12)			
Direct bilirubin; withdrawal visit; n= 79	0.0 (± 1.15)			
Direct bilirubin; follow up visit; n= 60	-0.2 (± 0.98)			
Total bilirubin; visit 1 (Screening); n= 83	2.5 (± 3.78)			
Total bilirubin; visit 2 (Week 13); n= 87	1.8 (± 4.28)			
Total bilirubin; visit 3 (Week 26); n= 76	1.8 (± 3.78)			
Total bilirubin; visit 4 (Week 39); n= 70	2.1 (± 4.46)			
Total bilirubin; visit 5 (Week 52); n= 65	2.6 (± 4.26)			
Total bilirubin; visit 6 (Week 69); n= 62	1.8 (± 4.21)			
Total bilirubin; visit 7 (Week 86); n= 54	1.4 (± 4.41)			
Total bilirubin; visit 8 (Week 104); n= 42	1.8 (± 3.28)			
Total bilirubin; visit 9 (Week 121); n= 39	1.1 (± 3.59)			
Total bilirubin; visit 10 (Week 138); n= 36	1.6 (± 6.50)			
Total bilirubin; visit 11 (Week 156); n= 30	0.5 (± 2.99)			
Total bilirubin; visit 12 (Week 173); n= 23	0.6 (± 2.81)			
Total bilirubin; visit 13 (Week 190); n= 19	0.2 (± 4.26)			
Total bilirubin; visit 14 (Week 208); n= 10	0.3 (± 3.27)			
Total bilirubin; visit 15 (Week 225); n= 5	0.8 (± 2.17)			
Total bilirubin; visit 16 (Week 242); n= 4	1.3 (± 1.89)			
Total bilirubin; visit 17 (Week 260); n= 4	-0.3 (± 2.63)			
Total bilirubin; visit 18 (Week 277); n= 2	1.5 (± 0.71)			
Total bilirubin; withdrawal visit; n= 79	1.2 (± 3.75)			
Total bilirubin; follow up visit; n= 60	-0.8 (± 3.97)			
Creatinine; visit 1 (Screening); n= 82	3.68 (± 9.813)			
Creatinine; visit 2 (Week 13); n= 86	0.42 (± 8.033)			
Creatinine; visit 3 (Week 26); n= 74	0.65 (± 8.879)			
Creatinine; visit 4 (Week 39); n= 70	1.82 (± 9.716)			
Creatinine; visit 5 (Week 52); n= 65	1.40 (± 9.394)			
Creatinine; visit 6 (Week 69); n= 62	1.25 (± 8.980)			
Creatinine; visit 7 (Week 86); n= 54	0.55 (± 9.053)			
Creatinine; visit 8 (Week 104); n= 42	4.78 (± 8.921)			

Creatinine; visit 9 (Week 121); n= 39	3.67 (± 9.581)			
Creatinine; visit 10 (Week 138); n= 36	2.10 (± 11.317)			
Creatinine; visit 11 (Week 156); n= 30	5.33 (± 11.211)			
Creatinine; visit 12 (Week 173); n= 23	-0.93 (± 10.097)			
Creatinine; visit 13 (Week 190); n= 19	1.67 (± 11.314)			
Creatinine; visit 14 (Week 208); n= 10	-1.74 (± 13.636)			
Creatinine; visit 15 (Week 225); n= 5	2.08 (± 6.680)			
Creatinine; visit 16 (Week 242); n= 4	5.80 (± 8.844)			
Creatinine; visit 17 (Week 260); n= 4	9.23 (± 14.076)			
Creatinine; visit 18 (Week 277); n= 2	3.45 (± 8.697)			
Creatinine; withdrawal visit; n= 78	0.88 (± 8.920)			
Creatinine; follow up visit; n= 60	0.16 (± 9.873)			

Notes:

[34] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in BUN/creatinine ratio

End point title	Change from Baseline in BUN/creatinine ratio[35]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical chemistry parameters including BUN/creatinine ratio. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[36]			
Units: Ratio of BUN to creatinine				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 82	0.3 (± 20.71)			
Visit 2 (Week 13); n= 86	3.8 (± 23.49)			
Visit 3 (Week 26); n= 74	2.7 (± 20.38)			
Visit 4 (Week 39); n= 70	1.0 (± 23.43)			
Visit 5 (Week 52); n= 65	1.9 (± 27.30)			
Visit 6 (Week 69); n= 62	0.0 (± 22.69)			
Visit 7 (Week 86); n= 54	2.5 (± 24.05)			
Visit 8 (Week 104); n= 42	-2.5 (± 24.45)			

Visit 9 (Week 121); n= 39	0.6 (± 24.67)			
Visit 10 (Week 138); n= 36	0.2 (± 27.01)			
Visit 11 (Week 156); n= 30	-6.2 (± 24.68)			
Visit 12 (Week 173); n= 23	-5.7 (± 22.82)			
Visit 13 (Week 190); n= 19	1.1 (± 22.19)			
Visit 14 (Week 208); n= 10	-0.8 (± 23.37)			
Visit 15 (Week 225); n= 5	-8.8 (± 20.22)			
Visit 16 (Week 242); n= 4	4.0 (± 18.49)			
Visit 17 (Week 260); n= 4	2.0 (± 32.81)			
Visit 18 (Week 277); n= 2	3.0 (± 11.31)			
Withdrawal visit; n= 78	4.2 (± 23.96)			
Follow up visit; n= 60	0.4 (± 22.68)			

Notes:

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in calcium, chloride, CO2, glucose, potassium, magnesium, sodium and BUN

End point title	Change from Baseline in calcium, chloride, CO2, glucose, potassium, magnesium, sodium and BUN[37]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical chemistry parameters including calcium, chloride, CO2, glucose, potassium, magnesium, sodium and BUN. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[38]			
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Calcium; visit 1 (Screening); n= 82	-0.028 (± 0.0940)			
Calcium; visit 2 (Week 13); n= 86	-0.011 (± 0.1067)			
Calcium; visit 3 (Week 26); n= 74	-0.026 (± 0.1061)			
Calcium; visit 4 (Week 39); n= 69	-0.025 (± 0.1024)			
Calcium; visit 5 (Week 52); n= 64	-0.026 (± 0.1100)			
Calcium; visit 6 (Week 69); n= 61	-0.019 (± 0.0942)			

Calcium; visit 7 (Week 86); n= 54	-0.016 (± 0.0911)			
Calcium; visit 8 (Week 104); n= 42	-0.008 (± 0.0975)			
Calcium; visit 9 (Week 121); n= 39	-0.024 (± 0.1096)			
Calcium; visit 10 (Week 138); n= 36	-0.038 (± 0.1335)			
Calcium; visit 11 (Week 156); n= 30	-0.053 (± 0.1181)			
Calcium; visit 12 (Week 173); n= 23	-0.059 (± 0.1031)			
Calcium; visit 13 (Week 190); n= 19	-0.074 (± 0.1000)			
Calcium; visit 14 (Week 208); n= 10	-0.094 (± 0.0950)			
Calcium; visit 15 (Week 225); n= 5	-0.108 (± 0.0858)			
Calcium; visit 16 (Week 242); n= 4	-0.093 (± 0.0877)			
Calcium; visit 17 (Week 260); n= 4	-0.073 (± 0.0670)			
Calcium; visit 18 (Week 277); n= 2	-0.125 (± 0.02122)			
Calcium; withdrawal visit; n= 78	-0.033 (± 0.1148)			
Calcium; follow up visit; n= 60	-0.050 (± 0.1059)			
Chloride; visit 1 (Screening); n= 83	0.5 (± 2.88)			
Chloride; visit 2 (Week 13); n= 87	0.4 (± 2.73)			
Chloride; visit 3 (Week 26); n=75	0.1 (± 2.79)			
Chloride; visit 4 (Week 39); n= 70	1.5 (± 2.80)			
Chloride; visit 5 (Week 52); n= 65	1.2 (± 3.58)			
Chloride; visit 6 (Week 69); n= 62	0.4 (± 2.68)			
Chloride; visit 7 (Week 86); n= 54	1.5 (± 3.34)			
Chloride; visit 8 (Week 104); n= 42	1.3 (± 2.83)			
Chloride; visit 9 (Week 121); n= 39	1.4 (± 3.28)			
Chloride; visit 10 (Week 138); n= 36	1.2 (± 3.35)			
Chloride; visit 11 (Week 156); n= 30	2.0 (± 2.99)			
Chloride; visit 12 (Week 173); n= 23	1.6 (± 2.74)			
Chloride; visit 13 (Week 190); n= 19	2.4 (± 2.09)			
Chloride; visit 14 (Week 208); n= 10	1.2 (± 2.49)			
Chloride; visit 15 (Week 225); n= 5	1.2 (± 3.11)			
Chloride; visit 16 (Week 242); n= 4	2.0 (± 2.00)			
Chloride; visit 17 (Week 260); n= 4	3.5 (± 3.11)			
Chloride; visit 18 (Week 277); n= 2	-0.5 (± 0.71)			
Chloride; withdrawal visit; n= 79	0.6 (± 2.89)			
Chloride; follow up visit; n= 60	0.0 (± 2.79)			
CO2; visit 1 (Screening); n= 82	-0.2 (± 3.07)			
CO2; visit 2 (Week 13); n= 86	0.3 (± 2.42)			
CO2; visit 3 (Week 26); n= 74	0.5 (± 2.82)			
CO2; visit 4 (Week 39); n= 69	-0.2 (± 3.03)			
CO2; visit 5 (Week 52); n= 64	-0.2 (± 2.88)			
CO2; visit 6 (Week 69); n= 61	-0.5 (± 2.99)			
CO2; visit 7 (Week 86); n= 54	-0.6 (± 2.71)			
CO2; visit 8 (Week 104); n= 42	-0.6 (± 2.64)			

CO2; visit 9 (Week 121); n= 39	-1.0 (± 3.02)			
CO2; visit 10 (Week 138); n= 36	-0.9 (± 3.42)			
CO2; visit 11 (Week 156); n= 30	-1.0 (± 2.48)			
CO2; visit 12 (Week 173); n= 23	-0.9 (± 2.80)			
CO2; visit 13 (Week 190); n= 19	-1.5 (± 3.39)			
CO2; visit 14 (Week 208); n= 10	-3.6 (± 4.53)			
CO2; visit 15 (Week 225); n= 5	-2.4 (± 1.82)			
CO2; visit 16 (Week 242); n= 4	-1.0 (± 1.41)			
CO2; visit 17 (Week 260); n= 4	-0.5 (± 0.58)			
CO2; visit 18 (Week 277); n= 2	-0.5 (± 0.71)			
CO2; withdrawal visit; n= 78	0.0 (± 2.33)			
CO2; follow up visit; n= 60	-0.8 (± 2.92)			
Glucose; visit 1 (Screening); n= 83	0.20 (± 1.303)			
Glucose; visit 2 (Week 13); n= 87	0.16 (± 0.933)			
Glucose; visit 3 (Week 26); n= 75	0.17 (± 0.765)			
Glucose; visit 4 (Week 39); n= 70	0.40 (± 1.259)			
Glucose; visit 5 (Week 52); n= 65	0.23 (± 0.814)			
Glucose; visit 6 (Week 69); n= 62	0.25 (± 1.103)			
Glucose; visit 7 (Week 86); n= 54	0.21 (± 0.985)			
Glucose; visit 8 (Week 104); n= 42	0.21 (± 0.679)			
Glucose; visit 9 (Week 121); n= 39	0.31 (± 1.073)			
Glucose; visit 10 (Week 138); n= 36	0.30 (± 1.007)			
Glucose; visit 11 (Week 156); n= 30	0.10 (± 0.511)			
Glucose; visit 12 (Week 173); n= 23	-0.03 (± 0.820)			
Glucose; visit 13 (Week 190); n= 19	0.21 (± 1.446)			
Glucose; visit 14 (Week 208); n= 10	0.15 (± 0.412)			
Glucose; visit 15 (Week 225); n= 5	0.38 (± 0.981)			
Glucose; visit 16 (Week 242); n= 4	1.95 (± 3.313)			
Glucose; visit 17 (Week 260); n= 4	-0.10 (± 0.648)			
Glucose; visit 18 (Week 277); n= 2	-0.30 (± 0.141)			
Glucose; withdrawal visit; n= 79	0.14 (± 1.035)			
Glucose; follow up visit; n= 60	0.39 (± 1.162)			
Potassium; visit 1 (Screening); n= 82	-0.04 (± 0.467)			
Potassium; visit 2 (Week 13); n= 86	-0.07 (± 0.403)			
Potassium; visit 3 (Week 26); n= 74	-0.09 (± 0.453)			
Potassium; visit 4 (Week 39); n= 69	-0.11 (± 0.432)			
Potassium; visit 5 (Week 52); n= 64	-0.13 (± 0.430)			
Potassium; visit 6 (Week 69); n= 61	-0.21 (± 0.420)			
Potassium; visit 7 (Week 86); n= 54	-0.13 (± 0.411)			
Potassium; visit 8 (Week 104); n= 42	-0.05 (± 0.433)			
Potassium; visit 9 (Week 121); n= 39	-0.09 (± 0.376)			
Potassium; visit 10 (Week 138); n= 36	-0.07 (± 0.388)			

Potassium; visit 11 (Week 156); n= 30	-0.16 (± 0.390)			
Potassium; visit 12 (Week 173); n= 23	-0.13 (± 0.411)			
Potassium; visit 13 (Week 190); n= 19	-0.02 (± 0.351)			
Potassium; visit 14 (Week 208); n= 10	-0.16 (± 0.430)			
Potassium; visit 15 (Week 225); n= 5	0.14 (± 0.321)			
Potassium; visit 16 (Week 242); n= 4	0.30 (± 0.294)			
Potassium; visit 17 (Week 260); n= 4	0.25 (± 0.351)			
Potassium; visit 18 (Week 277); n= 2	0.10 (± 0.424)			
Potassium; withdrawal visit; n= 78	-0.04 (± 0.367)			
Potassium; follow up visit; n= 60	-0.20 (± 0.478)			
Magnesium; visit 1 (Screening); n= 83	-0.017 (± 0.0576)			
Magnesium; visit 2 (Week 13); n= 87	-0.012 (± 0.0558)			
Magnesium; visit 3 (Week 26); n= 75	-0.007 (± 0.0619)			
Magnesium; visit 4 (Week 39); n= 70	-0.004 (± 0.0580)			
Magnesium; visit 5 (Week 52); n= 65	-0.008 (± 0.0625)			
Magnesium; visit 6 (Week 69); n= 62	-0.012 (± 0.0599)			
Magnesium; visit 7 (Week 86); n= 54	-0.018 (± 0.0627)			
Magnesium; visit 8 (Week 104); n= 42	0.007 (± 0.0632)			
Magnesium; visit 9 (Week 121); n= 39	-0.011 (± 0.0763)			
Magnesium; visit 10 (Week 138); n= 36	-0.007 (± 0.0543)			
Magnesium; visit 11 (Week 156); n= 30	0.005 (± 0.0651)			
Magnesium; visit 12 (Week 173); n= 23	-0.003 (± 0.0688)			
Magnesium; visit 13 (Week 190); n= 19	0.000 (± 0.0627)			
Magnesium; visit 14 (Week 208); n= 10	-0.013 (± 0.0579)			
Magnesium; visit 15 (Week 225); n= 5	0.000 (± 0.0474)			
Magnesium; visit 16 (Week 242); n= 4	-0.008 (± 0.1075)			
Magnesium; visit 17 (Week 260); n= 4	0.053 (± 0.1258)			
Magnesium; visit 18 (Week 277); n= 2	0.070 (± 0.0424)			
Magnesium; withdrawal visit; n= 79	-0.003 (± 0.0763)			
Magnesium; follow up visit; n= 60	-0.007 (± 0.0727)			
Sodium; visit 1 (Screening); n= 83	0.2 (± 2.88)			
Sodium; visit 2 (Week 13); n= 80	0.2 (± 2.83)			
Sodium; visit 3 (Week 26); n= 69	-0.2 (± 2.79)			
Sodium; visit 4 (Week 39); n= 64	0.7 (± 2.37)			

Sodium; visit 5 (Week 52); n= 59	0.5 (± 3.35)			
Sodium; visit 6 (Week 69); n= 58	-0.2 (± 2.34)			
Sodium; visit 7 (Week 86); n= 51	0.6 (± 3.03)			
Sodium; visit 8 (Week 104); n= 39	0.9 (± 2.28)			
Sodium; visit 9 (Week 121); n= 36	0.7 (± 2.78)			
Sodium; visit 10 (Week 138); n= 35	0.3 (± 3.06)			
Sodium; visit 11 (Week 156); n= 28	0.9 (± 3.47)			
Sodium; visit 12 (Week 173); n= 21	0.7 (± 3.38)			
Sodium; visit 13 (Week 190); n= 17	0.6 (± 1.73)			
Sodium; visit 14 (Week 208); n= 10	-1.2 (± 1.03)			
Sodium; visit 15 (Week 225); n= 5	-0.4 (± 1.52)			
Sodium; visit 16 (Week 242); n= 4	-0.8 (± 1.89)			
Sodium; visit 17 (Week 260); n= 4	0.8 (± 2.63)			
Sodium; visit 18 (Week 277); n= 2	-1.0 (± 0.00)			
Sodium; withdrawal visit; n= 71	0.2 (± 2.85)			
Sodium; follow up visit; n= 53	-0.7 (± 2.45)			
BUN; visit 1 (Screening); n= 83	0.32 (± 1.317)			
BUN; visit 2 (Week 13); n= 80	0.44 (± 1.483)			
BUN; visit 3 (Week 26); n= 69	0.31 (± 1.287)			
BUN; visit 4 (Week 39); n= 64	0.22 (± 1.322)			
BUN; visit 5 (Week 52); n= 59	0.37 (± 1.643)			
BUN; visit 6 (Week 69); n= 58	0.13 (± 1.329)			
BUN; visit 7 (Week 86); n= 51	0.22 (± 1.467)			
BUN; visit 8 (Week 104); n= 39	0.22 (± 1.477)			
BUN; visit 9 (Week 121); n= 36	0.35 (± 1.444)			
BUN; visit 10 (Week 138); n= 35	0.18 (± 1.578)			
BUN; visit 11 (Week 156); n= 28	-0.06 (± 1.515)			
BUN; visit 12 (Week 173); n= 21	-0.40 (± 1.362)			
BUN; visit 13 (Week 190); n= 17	0.23 (± 1.088)			
BUN; visit 14 (Week 208); n= 10	-0.11 (± 1.604)			
BUN; visit 15 (Week 225); n= 5	-0.40 (± 1.416)			
BUN; visit 16 (Week 242); n= 4	0.80 (± 0.707)			
BUN; visit 17 (Week 260); n= 4	1.10 (± 2.889)			
BUN; visit 18 (Week 277); n= 2	0.50 (± 0.141)			
BUN; withdrawal visit; n= 71	0.49 (± 1.450)			
BUN; follow up visit; n= 53	0.14 (± 1.468)			

Notes:

[38] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in absolute basophils, absolute eosinophils, absolute lymphocytes, absolute monocytes, absolute total neutrophils, platelet count and WBC count

End point title	Change from Baseline in absolute basophils, absolute eosinophils, absolute lymphocytes, absolute monocytes, absolute total neutrophils, platelet count and WBC count[39]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including absolute basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelet count and WBC count. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[40]			
Units: Giga cells per liter (GI/L)				
arithmetic mean (standard deviation)				
Basophils; visit 1 (Screening); n= 84	-0.001 (± 0.0203)			
Basophils; visit 2 (Week 13); n= 85	-0.005 (± 0.0159)			
Basophils; visit 3 (Week 26); n= 71	-0.003 (± 0.0197)			
Basophils; visit 4 (Week 39); n= 65	0.001 (± 0.0231)			
Basophils; visit 5 (Week 52); n= 60	0.002 (± 0.0170)			
Basophils; visit 6 (Week 69); n= 58	-0.002 (± 0.0202)			
Basophils; visit 7 (Week 86); n= 53	-0.002 (± 0.0188)			
Basophils; visit 8 (Week 104); n= 36	0.003 (± 0.0165)			
Basophils; visit 9 (Week 121); n= 35	-0.002 (± 0.0183)			
Basophils; visit 10 (Week 138); n= 33	-0.002 (± 0.0142)			
Basophils; visit 11 (Week 156); n= 29	-0.001 (± 0.0151)			
Basophils; visit 12 (Week 173); n= 24	-0.004 (± 0.0125)			
Basophils; visit 13 (Week 190); n= 17	0.000 (± 0.0255)			
Basophils; visit 14 (Week 208); n= 10	-0.004 (± 0.0165)			
Basophils; visit 15 (Week 225); n= 4	-0.010 (± 0.0115)			
Basophils; visit 16 (Week 242); n= 4	-0.003 (± 0.0050)			
Basophils; visit 17 (Week 260); n= 4	-0.005 (± 0.0129)			
Basophils; visit 18 (Week 277); n= 2	0.000 (± 0.0000)			
Basophils; withdrawal visit; n= 78	0.001 (± 0.0186)			
Basophils; follow up visit; n= 56	-0.008 (± 0.0190)			

Eosinophils; visit 1 (Screening); n= 84	-0.011 (± 0.1103)			
Eosinophils; visit 2 (Week 13); n= 85	-0.018 (± 0.2505)			
Eosinophils; visit 3 (Week 26); n= 71	-0.029 (± 0.2191)			
Eosinophils; visit 4 (Week 39); n= 65	-0.050 (± 0.2523)			
Eosinophils; visit 5 (Week 52); n= 60	-0.065 (± 0.3016)			
Eosinophils; visit 6 (Week 69); n= 58	-0.025 (± 0.1586)			
Eosinophils; visit 7 (Week 86); n= 53	-0.016 (± 0.1585)			
Eosinophils; visit 8 (Week 104); n= 36	-0.020 (± 0.1992)			
Eosinophils; visit 9 (Week 121); n= 35	-0.015 (± 0.1721)			
Eosinophils; visit 10 (Week 138); n= 33	-0.052 (± 0.1918)			
Eosinophils; visit 11 (Week 156); n= 29	-0.046 (± 0.1846)			
Eosinophils; visit 12 (Week 173); n= 24	-0.065 (± 0.3068)			
Eosinophils; visit 13 (Week 190); n= 17	-0.104 (± 0.3376)			
Eosinophils; visit 14 (Week 208); n= 10	-0.158 (± 0.1591)			
Eosinophils; visit 15 (Week 225); n= 4	-0.140 (± 0.0589)			
Eosinophils; visit 16 (Week 242); n= 4	-0.070 (± 0.1131)			
Eosinophils; visit 17 (Week 260); n= 4	-0.055 (± 0.0850)			
Eosinophils; visit 18 (Week 277); n= 2	0.005 (± 0.0636)			
Eosinophils; withdrawal visit; n= 78	-0.056 (± 0.2713)			
Eosinophils; follow up visit; n= 56	-0.091 (± 0.3022)			
Lymphocytes; visit 1 (Screening); n= 84	-0.225 (± 0.6631)			
Lymphocytes; visit 2 (Week 13); n= 85	-0.170 (± 0.5506)			
Lymphocytes; visit 3 (Week 26); n= 71	-0.133 (± 0.6123)			
Lymphocytes; visit 4 (Week 39); n= 65	-0.210 (± 0.5412)			
Lymphocytes; visit 5 (Week 52); n= 60	-0.214 (± 0.6446)			
Lymphocytes; visit 6 (Week 69); n= 58	-0.178 (± 0.5194)			
Lymphocytes; visit 7 (Week 86); n= 53	-0.093 (± 0.5793)			
Lymphocytes; visit 8 (Week 104); n= 36	-0.111 (± 0.5839)			
Lymphocytes; visit 9 (Week 121); n= 35	0.008 (± 0.8295)			
Lymphocytes; visit 10 (Week 138); n= 33	-0.177 (± 0.6622)			
Lymphocytes; visit 11 (Week 156); n= 29	-0.324 (± 0.6801)			

Lymphocytes; visit 12 (Week 173); n= 24	-0.226 (± 0.5720)			
Lymphocytes; visit 13 (Week 190); n= 17	-0.325 (± 0.7086)			
Lymphocytes; visit 14 (Week 208); n= 10	-0.354 (± 0.6563)			
Lymphocytes; visit 15 (Week 225); n= 4	-0.990 (± 0.6633)			
Lymphocytes; visit 16 (Week 242); n= 4	-0.818 (± 0.9694)			
Lymphocytes; visit 17 (Week 260); n= 4	-0.993 (± 0.7200)			
Lymphocytes; visit 18 (Week 277); n= 2	-1.465 (± 0.6718)			
Lymphocytes; withdrawal visit; n= 78	-0.153 (± 0.6466)			
Lymphocytes; follow up visit; n= 56	-0.081 (± 0.7105)			
Monocytes; visit 1 (Screening); n= 84	-0.043 (± 0.1800)			
Monocytes; visit 2 (Week 13); n= 85	-0.009 (± 0.1603)			
Monocytes; visit 3 (Week 26); n= 71	0.039 (± 0.2031)			
Monocytes; visit 4 (Week 39); n= 65	-0.005 (± 0.1940)			
Monocytes; visit 5 (Week 52); n= 60	-0.006 (± 0.1876)			
Monocytes; visit 6 (Week 69); n= 58	0.018 (± 0.1697)			
Monocytes; visit 7 (Week 86); n= 53	0.055 (± 0.2375)			
Monocytes; visit 8 (Week 104); n= 36	-0.032 (± 0.1911)			
Monocytes; visit 9 (Week 121); n= 35	0.023 (± 0.1777)			
Monocytes; visit 10 (Week 138); n= 33	0.005 (± 0.1796)			
Monocytes; visit 11 (Week 156); n= 29	-0.028 (± 0.1982)			
Monocytes; visit 12 (Week 173); n= 24	-0.032 (± 0.1648)			
Monocytes; visit 13 (Week 190); n= 17	-0.078 (± 0.2279)			
Monocytes; visit 14 (Week 208); n= 10	-0.090 (± 0.2821)			
Monocytes; visit 15 (Week 225); n= 4	-0.037 (± 0.0450)			
Monocytes; visit 16 (Week 242); n= 4	-0.020 (± 0.0829)			
Monocytes; visit 17 (Week 260); n= 4	0.025 (± 0.1173)			
Monocytes; visit 18 (Week 277); n= 2	0.080 (± 0.0000)			
Monocytes; withdrawal visit; n= 78	0.041 (± 0.2417)			
Monocytes; follow up visit; n= 56	-0.021 (± 0.2091)			
Total neutrophils; visit 1 (Screening); n= 84	-0.108 (± 1.6418)			
Total neutrophils; visit 2 (Week 13); n= 85	-0.354 (± 1.4357)			

Total neutrophils; visit 3 (Week 26); n= 71	-0.175 (± 1.4304)			
Total neutrophils; visit 4 (Week 39); n= 65	-0.582 (± 1.5237)			
Total neutrophils; visit 5 (Week 52); n= 60	0.165 (± 1.9517)			
Total neutrophils; visit 6 (Week 69); n= 58	-0.159 (± 1.5356)			
Total neutrophils; visit 7 (Week 86); n= 53	-0.046 (± 2.0418)			
Total neutrophils; visit 8 (Week 104); n= 36	-0.403 (± 1.5416)			
Total neutrophils; visit 9 (Week 121); n= 35	0.519 (± 1.9016)			
Total neutrophils; visit 10 (Week 138); n= 33	0.412 (± 1.9080)			
Total neutrophils; visit 11 (Week 156); n= 29	0.361 (± 1.5062)			
Total neutrophils; visit 12 (Week 173); n= 24	0.144 (± 1.7867)			
Total neutrophils; visit 13 (Week 190); n= 17	0.669 (± 2.6453)			
Total neutrophils; visit 14 (Week 208); n= 10	0.113 (± 1.7471)			
Total neutrophils; visit 15 (Week 225); n= 4	-0.825 (± 1.9404)			
Total neutrophils; visit 16 (Week 242); n= 4	-1.183 (± 1.9538)			
Total neutrophils; visit 17 (Week 260); n= 4	-0.990 (± 2.1510)			
Total neutrophils; visit 18 (Week 277); n= 2	-2.210 (± 2.6446)			
Total neutrophils; withdrawal visit; n= 78	0.209 (± 1.6761)			
Total neutrophils; follow up visit; n= 56	0.095 (± 1.9626)			
Platelet count; visit 1 (Screening); n= 84	-1.7 (± 34.31)			
Platelet count; visit 2 (Week 13); n= 88	3.7 (± 38.83)			
Platelet count; visit 3 (Week 26); n= 73	5.1 (± 44.34)			
Platelet count; visit 4 (Week 39); n= 68	2.9 (± 45.75)			
Platelet count; visit 5 (Week 52); n= 63	4.1 (± 37.72)			
Platelet count; visit 6 (Week 69); n= 62	6.9 (± 39.48)			
Platelet count; visit 7 (Week 86); n= 55	1.5 (± 50.29)			
Platelet count; visit 8 (Week 104); n= 41	4.5 (± 43.95)			
Platelet count; visit 9 (Week 121); n= 35	8.7 (± 45.39)			
Platelet count; visit 10 (Week 138); n= 36	6.8 (± 42.37)			
Platelet count; visit 11 (Week 156); n= 31	1.9 (± 37.92)			
Platelet count; visit 12 (Week 173); n= 24	9.7 (± 37.95)			
Platelet count; visit 13 (Week 190); n= 18	7.0 (± 37.15)			
Platelet count; visit 14 (Week 208); n= 10	18.9 (± 69.95)			
Platelet count; visit 15 (Week 225); n= 4	-31.3 (± 11.15)			

Platelet count; visit 16 (Week 242); n= 4	-9.0 (± 63.92)			
Platelet count; visit 17 (Week 260); n= 4	-10.0 (± 61.60)			
Platelet count; visit 18 (Week 277); n= 2	-19.0 (± 100.41)			
Platelet count; withdrawal visit; n= 79	8.9 (± 43.88)			
Platelet count; follow up visit; n= 58	8.9 (± 54.58)			
WBC count; visit 1 (Screening); n= 84	0.30 (± 6.496)			
WBC count; visit 2 (Week 13); n= 78	-0.46 (± 1.512)			
WBC count; visit 3 (Week 26); n= 66	-0.24 (± 1.354)			
WBC count; visit 4 (Week 39); n= 59	-0.84 (± 1.627)			
WBC count; visit 5 (Week 52); n= 54	-0.05 (± 1.989)			
WBC count; visit 6 (Week 69); n= 54	-0.41 (± 1.637)			
WBC count; visit 7 (Week 86); n= 50	-0.12 (± 2.059)			
WBC count; visit 8 (Week 104); n= 33	-0.51 (± 1.666)			
WBC count; visit 9 (Week 121); n= 32	0.58 (± 1.968)			
WBC count; visit 10 (Week 138); n= 32	0.22 (± 2.106)			
WBC count; visit 11 (Week 156); n= 27	0.09 (± 1.805)			
WBC count; visit 12 (Week 173); n= 22	-0.15 (± 1.971)			
WBC count; visit 13 (Week 190); n= 15	0.43 (± 2.804)			
WBC count; visit 14 (Week 208); n= 10	-0.49 (± 2.247)			
WBC count; visit 15 (Week 225); n= 4	-2.00 (± 2.608)			
WBC count; visit 16 (Week 242); n= 4	-2.10 (± 2.825)			
WBC count; visit 17 (Week 260); n= 4	-2.03 (± 2.941)			
WBC count; visit 18 (Week 277); n= 2	-3.60 (± 3.394)			
WBC count; withdrawal visit; n= 70	0.13 (± 1.757)			
WBC count; follow up visit; n= 50	-0.05 (± 1.905)			

Notes:

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) levels

End point title	Change from Baseline in hemoglobin and mean corpuscle hemoglobin concentration (MCHC) levels[41]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including hemoglobin and MCHC. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified

data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[42]			
Units: G/L				
arithmetic mean (standard deviation)				
Hemoglobin; visit 1 (Screening); n= 85	-3.5 (± 6.75)			
Hemoglobin; visit 2 (Week 13); n= 89	-2.4 (± 7.87)			
Hemoglobin; visit 3 (Week 26); n= 74	-2.7 (± 7.59)			
Hemoglobin; visit 4 (Week 39); n= 69	-2.9 (± 9.09)			
Hemoglobin; visit 5 (Week 52); n= 64	-2.9 (± 9.51)			
Hemoglobin; visit 6 (Week 69); n= 62	-2.5 (± 9.83)			
Hemoglobin; visit 7 (Week 86); n= 55	-0.4 (± 8.75)			
Hemoglobin; visit 8 (Week 104); n= 41	-0.7 (± 8.35)			
Hemoglobin; visit 9 (Week 121); n= 36	-1.4 (± 8.68)			
Hemoglobin; visit 10 (Week 138); n= 36	0.1 (± 12.38)			
Hemoglobin; visit 11 (Week 156); n= 31	-3.4 (± 9.73)			
Hemoglobin; visit 12 (Week 173); n= 24	-2.2 (± 9.46)			
Hemoglobin; visit 13 (Week 190); n= 18	-4.3 (± 9.11)			
Hemoglobin; visit 14 (Week 208); n= 10	-8.0 (± 10.02)			
Hemoglobin; visit 15 (Week 225); n= 4	-6.0 (± 4.76)			
Hemoglobin; visit 16 (Week 242); n= 4	-9.5 (± 6.66)			
Hemoglobin; visit 17 (Week 260); n= 4	-8.0 (± 6.16)			
Hemoglobin; visit 18 (Week 277); n= 2	-10.5 (± 7.78)			
Hemoglobin; withdrawal visit; n= 79	-1.7 (± 9.69)			
Hemoglobin; follow up visit; n= 59	-2.3 (± 11.53)			
MCHC; visit 1 (Screening); n= 85	-2.1 (± 12.61)			
MCHC; visit 2 (Week 13); n= 89	1.4 (± 12.22)			
MCHC; visit 3 (Week 26); n= 74	-1.1 (± 11.50)			
MCHC; visit 4 (Week 39); n= 69	-4.6 (± 12.75)			
MCHC; visit 5 (Week 52); n= 64	-5.4 (± 13.35)			
MCHC; visit 6 (Week 69); n= 62	-4.8 (± 11.64)			
MCHC; visit 7 (Week 86); n= 55	-5.8 (± 9.79)			
MCHC; visit 8 (Week 104); n= 41	-9.1 (± 10.62)			
MCHC; visit 9 (Week 121); n= 36	-6.9 (± 11.74)			
MCHC; visit 10 (Week 138); n= 36	-9.6 (± 9.87)			
MCHC; visit 11 (Week 156); n= 31	-10.1 (± 11.76)			
MCHC; visit 12 (Week 173); n= 24	-10.7 (± 9.45)			
MCHC; visit 13 (Week 190); n= 18	-15.2 (± 9.24)			

MCHC; visit 14 (Week 208); n= 10	-21.5 (± 10.48)			
MCHC; visit 15 (Week 225); n= 4	-16.3 (± 7.59)			
MCHC; visit 16 (Week 242); n= 4	-14.5 (± 5.51)			
MCHC; visit 17 (Week 260); n= 4	-16.0 (± 8.25)			
MCHC; visit 18 (Week 277); n= 2	-4.5 (± 9.19)			
MCHC; withdrawal visit; n= 79	-6.8 (± 9.61)			
MCHC; follow up visit; n= 59	-8.6 (± 10.18)			

Notes:

[42] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematocrit levels

End point title	Change from Baseline in hematocrit levels[43]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including hematocrit. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[44]			
Units: Proportion of red blood cells in blood				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 85	-0.0080 (± 0.02259)			
Visit 2 (Week 13); n= 89	-0.0087 (± 0.02508)			
Visit 3 (Week 26); n= 74	-0.0066 (± 0.02651)			
Visit 4 (Week 39); n= 69	-0.0030 (± 0.02861)			
Visit 5 (Week 52); n= 64	-0.0020 (± 0.02985)			
Visit 6 (Week 69); n= 62	-0.0020 (± 0.02821)			
Visit 7 (Week 86); n= 55	0.0063 (± 0.02627)			
Visit 8 (Week 104); n= 41	0.0103 (± 0.02839)			
Visit 9 (Week 121); n= 36	0.0053 (± 0.02819)			

Visit 10 (Week 138); n= 36	0.0129 (± 0.04091)			
Visit 11 (Week 156); n= 31	0.0025 (± 0.02755)			
Visit 12 (Week 173); n= 24	0.0070 (± 0.03167)			
Visit 13 (Week 190); n= 18	0.0061 (± 0.02857)			
Visit 14 (Week 208); n= 10	0.0015 (± 0.03213)			
Visit 15 (Week 225); n= 4	0.0050 (± 0.01857)			
Visit 16 (Week 242); n= 4	-0.0097 (± 0.02017)			
Visit 17 (Week 260); n= 4	-0.0040 (± 0.00841)			
Visit 18 (Week 277); n= 2	-0.0270 (± 0.03677)			
Withdrawal visit; n= 79	0.0034 (± 0.02926)			
Follow up visit; n= 59	0.0039 (± 0.03501)			

Notes:

[44] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean corpuscle hemoglobin (MCH) levels

End point title	Change from Baseline in mean corpuscle hemoglobin (MCH) levels[45]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including MCH. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[46]			
Units: Picograms (Pg)				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 85	-0.17 (± 0.910)			
Visit 2 (Week 13); n= 89	-0.33 (± 1.058)			
Visit 3 (Week 26); n= 74	-0.47 (± 0.809)			

Visit 4 (Week 39); n= 69	-0.83 (± 1.238)			
Visit 5 (Week 52); n= 64	-0.77 (± 1.087)			
Visit 6 (Week 69); n= 62	-0.91 (± 1.317)			
Visit 7 (Week 86); n= 55	-0.99 (± 1.227)			
Visit 8 (Week 104); n= 41	-1.17 (± 1.503)			
Visit 9 (Week 121); n= 36	-1.11 (± 1.551)			
Visit 10 (Week 138); n= 36	-1.28 (± 1.282)			
Visit 11 (Week 156); n= 31	-1.44 (± 1.065)			
Visit 12 (Week 173); n= 24	-1.78 (± 1.380)			
Visit 13 (Week 190); n= 18	-1.90 (± 1.251)			
Visit 14 (Week 208); n= 10	-2.19 (± 1.883)			
Visit 15 (Week 225); n= 4	-2.00 (± 1.291)			
Visit 16 (Week 242); n= 4	-2.50 (± 1.669)			
Visit 17 (Week 260); n= 4	-1.83 (± 1.382)			
Visit 18 (Week 277); n= 2	-2.65 (± 0.354)			
Withdrawal visit; n= 79	-1.11 (± 1.305)			
Follow up visit; n= 59	-1.08 (± 1.437)			

Notes:

[46] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean corpuscle volume (MCV) and mean platelet volume (MPV) levels

End point title	Change from Baseline in mean corpuscle volume (MCV) and mean platelet volume (MPV) levels[47]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including MCV and MPV. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[48]			
Units: Femtoliter (fL)				
arithmetic mean (standard deviation)				
MCV (Screening); Visit 1; n= 85	0.0 (± 3.55)			
MCV; Visit 2 (Week 13); n= 89	-1.5 (± 3.63)			
MCV; Visit 3 (Week 26); n= 74	-1.0 (± 3.32)			
MCV; Visit 4 (Week 39); n= 69	-1.2 (± 3.62)			
MCV; Visit 5 (Week 52); n= 64	-0.8 (± 3.71)			
MCV; Visit 6 (Week 69); n= 62	-1.4 (± 4.29)			
MCV; Visit 7 (Week 86); n= 55	-1.2 (± 3.56)			
MCV; Visit 8 (Week 104); n= 41	-0.9 (± 4.75)			
MCV; Visit 9 (Week 121); n= 36	-1.4 (± 4.00)			
MCV; Visit 10 (Week 138); n= 36	-1.1 (± 4.30)			
MCV; Visit 11 (Week 156); n= 31	-1.5 (± 4.18)			
MCV; Visit 12 (Week 173); n= 24	-2.5 (± 4.64)			
MCV; Visit 13 (Week 190); n= 18	-1.2 (± 4.40)			
MCV; Visit 14 (Week 208); n= 10	-0.9 (± 4.48)			
MCV; Visit 15 (Week 225); n= 4	-1.5 (± 1.73)			
MCV; Visit 16 (Week 242); n= 4	-4.0 (± 3.92)			
MCV; Visit 17 (Week 260); n= 4	-1.3 (± 2.63)			
MCV; Visit 18 (Week 277); n= 2	-7.0 (± 4.24)			
MCV; Withdrawal visit; n= 79	-1.4 (± 4.14)			
MCV; Follow up visit; n= 59	-0.9 (± 4.39)			
MPV; visit 1 (Screening); n= 84	-0.12 (± 0.715)			
MPV: visit 2 (Week 13); n= 86	-0.10 (± 0.756)			
MPV: visit 3 (Week 26); n= 71	-0.08 (± 0.612)			
MPV; visit 4 (Week 39); n= 67	-0.17 (± 0.823)			
MPV; visit 5 (Week 52); n= 61	-0.06 (± 0.746)			
MPV; visit 6 (Week 69); n= 58	-0.03 (± 0.654)			
MPV; visit 7 (Week 86); n= 53	0.12 (± 0.786)			
MPV; visit 8 (Week 104); n= 38	0.01 (± 0.902)			
MPV: visit 9 (Week 121); n= 35	0.13 (± 0.788)			
MPV; visit 10 (Week 138); n= 34	0.06 (± 0.773)			
MPV; visit 11 (Week 156); n= 29	0.14 (± 0.728)			
MPV: visit 12 (Week 173); n= 24	0.04 (± 0.944)			
MPV; visit 13 (Week 190); n= 17	-0.09 (± 0.766)			
MPV; visit 14 (Week 208); n= 10	-0.37 (± 0.455)			
MPV; visit 15 (Week 225); n= 4	-0.33 (± 1.053)			
MPV; visit 16 (Week 242); n= 4	-0.75 (± 0.802)			
MPV; visit 17 (Week 260); n= 4	-0.17 (± 0.670)			
MPV; visit 18 (Week 277); n= 2	-1.15 (± 0.071)			

MPV; withdrawal visit; n= 78	0.19 (± 0.902)			
MPV; follow up visit; n= 57	0.12 (± 0.859)			

Notes:

[48] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in RBC count

End point title	Change from Baseline in RBC count[49]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including RBC count. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[50]			
Units: Tetra cells per liter (TI/L)				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 85	-0.10 (± 0.212)			
Visit 2 (Week 13); n= 89	-0.03 (± 0.255)			
Visit 3 (Week 26); n= 74	-0.03 (± 0.240)			
Visit 4 (Week 39); n= 69	0.01 (± 0.272)			
Visit 5 (Week 52); n= 64	0.00 (± 0.311)			
Visit 6 (Week 69); n= 62	0.04 (± 0.300)			
Visit 7 (Week 86); n= 55	0.12 (± 0.260)			
Visit 8 (Week 104); n= 41	0.14 (± 0.280)			
Visit 9 (Week 121); n= 36	0.11 (± 0.299)			
Visit 10 (Week 138); n= 36	0.19 (± 0.445)			
Visit 11 (Week 156); n= 31	0.09 (± 0.344)			
Visit 12 (Week 173); n= 24	0.18 (± 0.385)			
Visit 13 (Week 190); n= 18	0.12 (± 0.343)			
Visit 14 (Week 208); n= 10	0.05 (± 0.366)			
Visit 15 (Week 225); n= 4	0.13 (± 0.206)			
Visit 16 (Week 242); n= 4	0.10 (± 0.216)			
Visit 17 (Week 260); n= 4	0.00 (± 0.082)			
Visit 18 (Week 277); n= 2	0.05 (± 0.212)			
Withdrawal visit; n= 79	0.10 (± 0.327)			

Follow up visit; n= 59	0.07 (± 0.409)			

Notes:

[50] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in percent basophils, percent eosinophils, percent lymphocytes, percent monocytes, percent neutrophils and RBC distribution width (RDW) levels

End point title	Change from Baseline in percent basophils, percent eosinophils, percent lymphocytes, percent monocytes, percent neutrophils and RBC distribution width (RDW) levels[51]

End point description:

Blood samples were collected from participants for evaluation of change from Baseline in clinical hematology parameters including percent basophils, eosinophils, lymphocytes, monocytes, neutrophils and RDW. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[52]			
Units: Percent of blood components				
arithmetic mean (standard deviation)				
Percent basophils; visit 1 (Screening); n= 84	0.00 (± 0.312)			
Percent basophils; visit 2 (Week 13); n= 85	-0.06 (± 0.243)			
Percent basophils; visit 3 (Week 26); n= 71	-0.03 (± 0.305)			
Percent basophils; visit 4 (Week 39); n= 65	0.07 (± 0.393)			
Percent basophils; visit 5 (Week 52); n= 60	0.04 (± 0.279)			
Percent basophils; visit 6 (Week 69); n= 58	-0.02 (± 0.315)			
Percent basophils; visit 7 (Week 86); n= 53	-0.02 (± 0.302)			
Percent basophils; visit 8 (Week 104); n= 36	0.11 (± 0.271)			
Percent basophils; visit 9 (Week 121); n= 35	-0.06 (± 0.239)			
Percent basophils; visit 10 (Week 138); n= 33	-0.02 (± 0.255)			

Percent basophils; visit 11 (Week 156); n= 29	0.00 (± 0.267)			
Percent basophils; visit 12 (Week 173); n= 24	-0.06 (± 0.253)			
Percent basophils; visit 13 (Week 190); n= 17	-0.01 (± 0.339)			
Percent basophils; visit 14 (Week 208); n= 10	-0.03 (± 0.283)			
Percent basophils; visit 15 (Week 225); n= 4	0.00 (± 0.216)			
Percent basophils; visit 16 (Week 242); n= 4	0.03 (± 0.126)			
Percent basophils; visit 17 (Week 260); n= 4	0.03 (± 0.050)			
Percent basophils; visit 18 (Week 277); n= 2	0.25 (± 0.212)			
Percent basophils; withdrawal visit; n= 78	0.01 (± 0.291)			
Percent basophils; follow up visit; n= 56	-0.13 (± 0.304)			
Percent eosinophils; visit 1 (Screening); n= 84	-0.06 (± 1.745)			
Percent eosinophils; visit 2 (Week 13); n= 85	0.00 (± 3.214)			
Percent eosinophils; visit 3 (Week 26); n= 71	-0.29 (± 2.773)			
Percent eosinophils; visit 4 (Week 39); n= 65	-0.44 (± 3.339)			
Percent eosinophils; visit 5 (Week 52); n= 60	-0.77 (± 4.046)			
Percent eosinophils; visit 6 (Week 69); n= 58	-0.26 (± 2.630)			
Percent eosinophils; visit 7 (Week 86); n= 53	-0.30 (± 2.634)			
Percent eosinophils; visit 8 (Week 104); n= 36	-0.04 (± 3.003)			
Percent eosinophils; visit 9 (Week 121); n= 35	-0.47 (± 2.653)			
Percent eosinophils; visit 10 (Week 138); n= 33	-0.92 (± 2.942)			
Percent eosinophils; visit 11 (Week 156); n= 29	-0.79 (± 2.484)			
Percent eosinophils; visit 12 (Week 173); n= 24	-0.70 (± 5.548)			
Percent eosinophils; visit 13 (Week 190); n= 17	-1.38 (± 5.539)			
Percent eosinophils; visit 14 (Week 208); n= 10	-2.49 (± 2.975)			
Percent eosinophils; visit 15 (Week 225); n= 4	-1.53 (± 1.565)			
Percent eosinophils; visit 16 (Week 242); n= 4	-0.43 (± 1.628)			
Percent eosinophils; visit 17 (Week 260); n= 4	0.00 (± 1.359)			
Percent eosinophils; visit 18 (Week 277); n= 2	1.65 (± 0.636)			
Percent eosinophils; withdrawal visit; n= 78	-0.83 (± 3.466)			
Percent eosinophils; follow up visit; n= 56	-1.30 (± 3.804)			
Percent lymphocytes; visit 1 (Screening); n= 84	-2.21 (± 8.440)			

Percent lymphocytes; visit 2 (Week 13); n= 85	-0.40 (± 9.550)			
Percent lymphocytes; visit 3 (Week 26); n= 71	-1.14 (± 10.820)			
Percent lymphocytes; visit 4 (Week 39); n= 65	0.27 (± 9.306)			
Percent lymphocytes; visit 5 (Week 52); n= 60	-2.58 (± 11.216)			
Percent lymphocytes; visit 6 (Week 69); n= 58	-1.26 (± 8.119)			
Percent lymphocytes; visit 7 (Week 86); n= 53	-0.53 (± 11.226)			
Percent lymphocytes; visit 8 (Week 104); n= 36	0.69 (± 9.013)			
Percent lymphocytes; visit 9 (Week 121); n= 35	-2.27 (± 11.733)			
Percent lymphocytes; visit 10 (Week 138); n= 33	-3.91 (± 8.960)			
Percent lymphocytes; visit 11 (Week 156); n= 29	-4.52 (± 9.015)			
Percent lymphocytes; visit 12 (Week 173); n= 24	-3.19 (± 9.398)			
Percent lymphocytes; visit 13 (Week 190); n= 17	-4.73 (± 12.168)			
Percent lymphocytes; visit 14 (Week 208); n= 10	-3.72 (± 5.911)			
Percent lymphocytes; visit 15 (Week 225); n= 4	-6.58 (± 3.848)			
Percent lymphocytes; visit 16 (Week 242); n= 4	-3.88 (± 10.160)			
Percent lymphocytes; visit 17 (Week 260); n= 4	-5.85 (± 4.886)			
Percent lymphocytes; visit 18 (Week 277); n= 2	-8.10 (± 3.818)			
Percent lymphocytes; withdrawal visit; n= 78	-2.60 (± 10.978)			
Percent lymphocytes; follow up visit; n= 56	-0.81 (± 12.709)			
Percent monocytes; visit 1 (Screening); n= 84	-0.33 (± 3.048)			
Percent monocytes; visit 2 (Week 13); n= 85	0.27 (± 2.720)			
Percent monocytes; visit 3 (Week 26); n= 71	0.86 (± 3.274)			
Percent monocytes; visit 4 (Week 39); n= 65	0.76 (± 3.286)			
Percent monocytes; visit 5 (Week 52); n= 60	-0.01 (± 3.058)			
Percent monocytes; visit 6 (Week 69); n= 58	0.64 (± 2.834)			
Percent monocytes; visit 7 (Week 86); n= 53	0.94 (± 3.148)			
Percent monocytes; visit 8 (Week 104); n= 36	0.04 (± 3.458)			
Percent monocytes; visit 9 (Week 121); n= 35	-0.11 (± 2.895)			
Percent monocytes; visit 10 (Week 138); n= 33	0.15 (± 3.160)			
Percent monocytes; visit 11 (Week 156); n= 29	-0.27 (± 3.007)			
Percent monocytes; visit 12 (Week 173); n= 24	-0.44 (± 2.687)			

Percent monocytes; visit 13 (Week 190); n= 17	-1.43 (± 2.909)			
Percent monocytes; visit 14 (Week 208); n= 10	-0.71 (± 5.153)			
Percent monocytes; visit 15 (Week 225); n= 4	1.08 (± 1.090)			
Percent monocytes; visit 16 (Week 242); n= 4	1.25 (± 1.686)			
Percent monocytes; visit 17 (Week 260); n= 4	2.03 (± 2.219)			
Percent monocytes; visit 18 (Week 277); n= 2	4.20 (± 2.687)			
Percent monocytes; withdrawal visit; n= 78	0.48 (± 3.355)			
Percent monocytes; follow up visit; n= 56	-0.35 (± 3.293)			
Percent neutrophils; visit 1 (Screening); n= 84	2.60 (± 11.021)			
Percent neutrophils; visit 2 (Week 13); n= 85	0.19 (± 11.584)			
Percent neutrophils; visit 3 (Week 26); n= 71	0.60 (± 12.994)			
Percent neutrophils; visit 4 (Week 39); n= 65	-0.66 (± 11.810)			
Percent neutrophils; visit 5 (Week 52); n= 60	3.31 (± 14.222)			
Percent neutrophils; visit 6 (Week 69); n= 58	0.90 (± 10.552)			
Percent neutrophils; visit 7 (Week 86); n= 53	-0.09 (± 14.427)			
Percent neutrophils; visit 8 (Week 104); n= 37	-0.81 (± 11.595)			
Percent neutrophils; visit 9 (Week 121); n= 35	2.91 (± 14.604)			
Percent neutrophils; visit 10 (Week 138); n= 33	4.70 (± 12.464)			
Percent neutrophils; visit 11 (Week 156); n= 29	5.58 (± 10.691)			
Percent neutrophils; visit 12 (Week 173); n= 24	4.39 (± 13.509)			
Percent neutrophils; visit 13 (Week 190); n= 17	7.55 (± 16.056)			
Percent neutrophils; visit 14 (Week 208); n= 10	6.95 (± 7.643)			
Percent neutrophils; visit 15 (Week 225); n= 4	7.03 (± 5.900)			
Percent neutrophils; visit 16 (Week 242); n= 4	3.03 (± 10.460)			
Percent neutrophils; visit 17 (Week 260); n= 4	3.80 (± 3.990)			
Percent neutrophils; visit 18 (Week 277); n= 2	2.00 (± 7.354)			
Percent neutrophils; withdrawal visit; n= 78	2.94 (± 13.146)			
Percent neutrophils; follow up visit; n= 56	2.58 (± 14.680)			
RDW; visit 1 (Screening); n= 85	0.41 (± 1.398)			
RDW; visit 2 (Week 13); n= 89	-0.07 (± 1.532)			
RDW; visit 3 (Week 26); n= 74	0.05 (± 0.924)			
RDW; visit 4 (Week 39); n= 69	0.47 (± 1.637)			

RDW; visit 5 (Week 52); n= 64	0.35 (± 1.598)			
RDW; visit 6 (Week 69); n= 62	0.05 (± 1.437)			
RDW; visit 7 (Week 86); n= 55	0.05 (± 1.109)			
RDW; visit 8 (Week 104); n= 41	0.32 (± 1.386)			
RDW; visit 9 (Week 121); n= 36	-0.19 (± 1.084)			
RDW; visit 10 (Week 138); n= 36	0.22 (± 0.885)			
RDW; visit 11 (Week 156); n= 31	0.94 (± 1.760)			
RDW; visit 12 (Week 173); n= 24	0.41 (± 1.292)			
RDW; visit 13 (Week 190); n= 18	0.88 (± 0.919)			
RDW; visit 14 (Week 208); n= 10	1.98 (± 1.605)			
RDW; visit 15 (Week 225); n= 4	0.28 (± 0.550)			
RDW; visit 16 (Week 242); n= 4	3.95 (± 6.855)			
RDW; visit 17 (Week 260); n= 4	2.50 (± 2.202)			
RDW; visit 18 (Week 277); n= 2	2.05 (± 0.495)			
RDW; withdrawal visit; n= 79	0.10 (± 1.097)			
RDW; follow up visit; n= 59	0.27 (± 1.235)			

Notes:

[52] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine albumin creatinine ratio

End point title	Change from Baseline in urine albumin creatinine ratio[53]

End point description:

Urine samples were collected from participants for evaluation of change from Baseline in urinalysis parameters including albumin creatinine ratio. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[54]			
Units: Mg of urine albumin/ mmol of creatinine				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 39	-0.57 (± 3.573)			
Visit 2 (Week 13); n= 72	-0.07 (± 3.172)			
Visit 3 (Week 26); n= 54	0.15 (± 3.678)			
Visit 4 (Week 39); n= 53	-0.64 (± 3.241)			

Visit 5 (Week 52); n= 52	-0.69 (± 3.065)			
Visit 6 (Week 69); n= 46	-0.53 (± 3.489)			
Visit 7 (Week 86); n= 47	0.07 (± 6.062)			
Visit 8 (Week 104); n= 32	-0.75 (± 4.508)			
Visit 9 (Week 121); n= 30	-0.89 (± 5.421)			
Visit 10 (Week 138); n= 26	-1.05 (± 4.236)			
Visit 11 (Week 156); n= 22	-0.65 (± 2.494)			
Visit 12 (Week 173); n= 19	-1.81 (± 5.060)			
Visit 13 (Week 190); n= 10	-0.59 (± 1.748)			
Visit 14 (Week 208); n= 8	-1.70 (± 4.032)			
Visit 15 (Week 225); n= 4	0.13 (± 0.981)			
Visit 16 (Week 242); n= 3	-0.33 (± 0.153)			
Visit 17 (Week 260); n= 3	-0.33 (± 0.321)			
Visit 18 (Week 277); n= 2	-0.50 (± 0.990)			
Withdrawal visit; n= 63	-0.35 (± 3.874)			
Follow up visit; n= 48	-0.62 (± 3.515)			

Notes:

[54] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine albumin levels

End point title	Change from Baseline in urine albumin levels[55]

End point description:

Urine samples were collected from participants for evaluation of change from Baseline in urinalysis parameters including albumin levels. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[56]			
Units: Milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 39	-5.2 (± 57.64)			
Visit 2 (Week 13); n= 72	-1.8 (± 48.39)			
Visit 3 (Week 26); n= 54	-17.1 (± 92.34)			
Visit 4 (Week 39); n= 53	-21.0 (± 94.25)			
Visit 5 (Week 52); n= 52	-21.6 (± 94.87)			
Visit 6 (Week 69); n= 46	-15.7 (± 56.98)			
Visit 7 (Week 86); n= 47	7.7 (± 131.03)			
Visit 8 (Week 104); n= 32	-8.1 (± 59.50)			
Visit 9 (Week 121); n= 30	-14.7 (± 61.73)			
Visit 10 (Week 138); n= 26	-16.0 (± 66.79)			
Visit 11 (Week 156); n= 22	-7.4 (± 35.40)			
Visit 12 (Week 173); n= 19	-27.2 (± 80.24)			
Visit 13 (Week 190); n= 10	-2.8 (± 27.95)			
Visit 14 (Week 208); n= 8	-15.9 (± 45.76)			
Visit 15 (Week 225); n= 4	-1.8 (± 11.53)			
Visit 16 (Week 242); n= 3	-8.7 (± 9.61)			
Visit 17 (Week 260); n= 3	-3.3 (± 12.86)			
Visit 18 (Week 277); n= 2	-7.5 (± 0.71)			
Withdrawal visit; n= 63	-6.5 (± 51.69)			
Follow up visit; n= 48	-19.9 (± 99.24)			

Notes:

[56] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in urine creatinine levels

End point title	Change from baseline in urine creatinine levels[57]

End point description:

Urine samples were collected from participants for evaluation of change from Baseline in urinalysis parameters including creatinine levels. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[58]			
Units: µmol/L				
arithmetic mean (standard deviation)				
Visit 1 (Screening); n= 52	-2019.6 (± 10153.70)			
Visit 2 (Week 13); n= 89	-1846.2 (± 8206.65)			
Visit 3 (Week 26); n= 75	-3023.7 (± 9197.50)			
Visit 4 (Week 39); n= 66	-2849.6 (± 7810.79)			
Visit 5 (Week 52); n= 63	-1626.5 (± 10205.13)			
Visit 6 (Week 69); n= 59	-3534.2 (± 8657.09)			
Visit 7 (Week 86); n= 55	-2664.4 (± 7900.30)			
Visit 8 (Week 104); n= 42	-2645.1 (± 8368.43)			
Visit 9 (Week 121); n= 37	-1727.3 (± 10330.75)			
Visit 10 (Week 138); n= 35	-1712.6 (± 11352.03)			
Visit 11 (Week 156); n= 30	-1400.0 (± 13151.92)			
Visit 12 (Week 173); n= 23	-1008.3 (± 9395.56)			
Visit 13 (Week 190); n= 19	-3604.1 (± 10215.20)			
Visit 14 (Week 208); n= 10	3238.3 (± 12290.24)			
Visit 15 (Week 225); n= 5	-675.0 (± 16785.90)			
Visit 16 (Week 242); n= 4	-5426.3 (± 13280.49)			
Visit 17 (Week 260); n= 4	148.8 (± 15164.36)			
Visit 18 (Week 277); n= 2	-7337.5 (± 10850.55)			
Withdrawal visit; n= 80	-3570.3 (± 8244.65)			
Follow up visit; n= 60	-515.8 (± 9359.74)			

Notes:

[58] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Changes from Baseline in American Urological Association Symptom Scale

(AUA SS) score

End point title	Changes from Baseline in American Urological Association Symptom Scale (AUA SS) score[59]

End point description:

The effect of retigabine on bladder function was assessed using AUA symptom index. It is a 7-item Likert-scored scale ranging from 0 (no symptom at all) to 5 (almost always symptoms present) with a total possible score of 35. AUA SS score is the sum of the responses to these seven questions. The total score for all questions was classified as mild (0 to 7), moderate (8 to 19), or severe (>19). Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

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: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[60]			
Units: Score on AUA SS scale				
arithmetic mean (standard deviation)				
Visit 3 (Week 26); n= 82	-0.7 (± 3.50)			
Visit 5 (Week 52); n= 68	-0.9 (± 4.67)			
Visit 8 (Week 104); n= 42	-1.0 (± 3.79)			
Visit 11 (Week 156); n= 31	-1.0 (± 4.18)			
Visit 14 (Week 208); n= 10	-2.3 (± 5.54)			
Visit 17 (Week 260); n= 4	-6.5 (± 7.72)			
Withdrawal visit; n= 85	-1.0 (± 3.99)			

Notes:

[60] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Post-Void Residual (PVR) bladder ultrasound urine volume

End point title	Change from Baseline in Post-Void Residual (PVR) bladder ultrasound urine volume[61]

End point description:

The PVR bladder ultrasound was used to assess urinary retention. Baseline was defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Change from Baseline was defined as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline and up to 5.8 years

Notes:

[61] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[62]			
Units: Milliliter (mL)				
arithmetic mean (standard deviation)				
Visit 3 (Week 26); n= 77	-6.0 (± 24.73)			
Visit 5 (Week 52); n= 64	2.7 (± 49.20)			
Visit 8 (Week 104); n= 40	3.9 (± 49.03)			
Visit 11 (Week 156); n= 25	2.0 (± 18.40)			
Visit 14 (Week 208); n= 10	-16.0 (± 21.33)			
Visit 17 (Week 260); n= 4	-23.3 (± 25.00)			
Withdrawal visit; n= 67	-7.6 (± 30.39)			

Notes:

[62] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with suicidal ideation or behavior assessed by the Columbia Suicide Severity Rating Scale (C-SSRS) score

End point title	Number of participants with suicidal ideation or behavior assessed by the Columbia Suicide Severity Rating Scale (C-SSRS) score[63]

End point description:

Number of participants with suicidal ideation or behavior during treatment were assessed using the C-SSRS score scale. It is 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. Participants are classified with respect to extent of suicidal ideation, extent of suicidal behavior, and with respect to self-injurious behavior.

End point type	Primary

End point timeframe:

Up to 5.8 years

Notes:

[63] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	95[64]			
Units: Participants				
Suicidal ideation	1			
Suicidal behavior	0			
Self-injurious behavior, no suicidal attempt	0			

Notes:

[64] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants experiencing new seizure types

End point title	Number of participants experiencing new seizure types[65]

End point description:

Number of participants experiencing new seizure type that is seizure not experienced before were summarized. New seizure types were classified into 5 classes including type A (simple partial seizure), type B (complex partial seizure), type C (Partials, evolving to Secondary Generalized Seizures), type D (Generalized, excluding Myoclonic Seizures), type D2 (Myoclonic Seizures) and type E (Unclassified Seizures).

End point type	Primary

End point timeframe:

Up to 5.8 years

Notes:

[65] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[66]			
Units: Participants				
Type A; Simple Partial Seizures	5			
Type B; Complex Partial Seizures	2			
Type C; Partials, evolving to Sec. Gen. Seizures	0			
Type D; Generalized, excl. Myoclonic Seizures	0			
Type D2; Myoclonic Seizures	0			
Type E; Unclassified seizures	0			

Notes:

[66] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants experiencing worsening of seizures

End point title	Number of participants experiencing worsening of seizures[67]

End point description:

Worsening of seizures was defined as an increase in seizure frequency or the occurrence of a new, more severe seizure type, or status epilepticus occurring in a participant without a history of status epilepticus. An increase in seizure frequency was defined as doubling of the 28-day seizure frequency compared to the 28-day Baseline seizure frequency established in the parent study. Number of participants experiencing worsening of seizure during study period are presented.

End point type	Primary

End point timeframe:

Up to 5.8 years

Notes:

[67] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[68]			
Units: Participants				
Participants	1			

Notes:

[68] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Duration of retigabine exposure

End point title	Duration of retigabine exposure[69]

End point description:

Duration of exposure was calculated from the first dose through the last dose during study including the Taper Phase and presented using median and full range.

End point type	Primary

End point timeframe:

Up to 5.8 years

Notes:

[69] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[70]			
Units: Weeks				
median (full range (min-max))				
Weeks	103.7 (0.5 to 284)			

Notes:

[70] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Resolution of Abnormal Eye Pigmentation After Discontinuation of Retigabine

End point title	Number of Participants With Resolution of Abnormal Eye Pigmentation After Discontinuation of Retigabine[71]

End point description:

The ophthalmologist/retina specialist determined the presence or absence of retinal and non-retinal ocular abnormalities. Retinal abnormalities included abnormalities in the macula and/or the peripheral retina and non-retinal ocular pigmentary abnormality.

End point type	Primary

End point timeframe:

Up to 2.6 years

Notes:

[71] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	9[72]			
Units: Participants				
number (not applicable)				
Retinal pigmentary abnormality	1			
Non-retinal ocular pigmentary abnormality	1			

Notes:

[72] - All SFUCP Subjects

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Resolution of Dermatologist Confirmed Abnormal Discoloration After Discontinuation of Retigabine

End point title	Number of Participants With Resolution of Dermatologist Confirmed Abnormal Discoloration After Discontinuation of Retigabine[73]

End point description:

Participants who enter the SFUCP who had an on-treatment finding(s) of abnormal discoloration of skin, lips, nails or mucosa confirmed by a dermatologist entered the SFUCP and underwent assessments performed by a dermatologist at 6-monthly intervals. The assessment of the participant's skin included assessment of the skin around the eyes and the eyelids, lips, nails, and mucosa.

End point type	Primary

End point timeframe:

Up to 2.6 years

Notes:

[73] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	9[74]			
Units: Participants				
number (not applicable)	2			

Notes:

[74] - All SFUCP Subjects

Statistical analyses

No statistical analyses for this end point

Primary: Time From Discontinuation of Retigabine to Resolution of Abnormal Eye Pigmentation

End point title	Time From Discontinuation of Retigabine to Resolution of

	Abnormal Eye Pigmentation[75]

End point description:

Retinal pigmentary abnormality was determined by either an ophthalmologist or retina specialist. Retinal pigmentary abnormality included abnormality of macula, peripheral retina and unspecified location. If a participant had pigmentary abnormality of macula and pigmentary abnormality of the peripheral retina both should be resolved in order for retinal pigmentary abnormality to be considered resolved. If a participant had non-retinal ocular pigmentary abnormality in more than one location (conjunctiva, sclera, cornea, iris or lens), all should be resolved for non-retinal pigmentary abnormality to be considered resolved.

End point type	Primary

End point timeframe:

Up to 2.6 years

Notes:

[75] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	1[76]			
Units: Days				
median (full range (min-max))				
Retinal Pigmentary Abnormality	157.0 (157 to 157)			
Non-Retinal Ocular Pigmentary Abnormality	119.0 (119 to 119)			

Notes:

[76] - All SFUCP Subjects

Statistical analyses

No statistical analyses for this end point

Primary: Time From Discontinuation of Retigabine to Resolution of All Dermatologist-Confirmed Abnormal Discoloration

End point title	Time From Discontinuation of Retigabine to Resolution of All Dermatologist-Confirmed Abnormal Discoloration[77]

End point description:

Assessments were at approximately 6-monthly intervals (timed relative to the participants previous dermatology assessment) until the abnormal discoloration either resolved or stabilized (as defined by no changes over 2 consecutive 6-monthly assessments performed by the dermatologist over at least 12 months after discontinuation of retigabine). The assessment of the participant's skin included assessment of the skin around the eyes and the eyelids, lips, nails, and mucosa. Only participants with resolution of the specified tissue are included in this analysis. 99999 indicates data was not available due to low number of participants.

End point type	Primary

End point timeframe:

Up to 2.6 years

Notes:

[77] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	9[78]			
Units: Days				
median (full range (min-max))				
All; n= 2	582.0 (253 to 911)			
Skin; n= 1	192.0 (192 to 192)			
Lips; n= 0	99999 (99999 to 99999)			
Nails; n= 1	253.0 (253 to 253)			
Mucosa; n= 3	701.0 (192 to 911)			

Notes:

[78] - All SFUCP Subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants experiencing a 0 to <25, 25 to <50, 50 to <75 and 75 to 100 percent reduction in 28 day POS frequency from Baseline

End point title	Number of participants experiencing a 0 to <25, 25 to <50, 50 to <75 and 75 to 100 percent reduction in 28 day POS frequency from Baseline

End point description:

The seizure frequency was recorded in daily seizure calendar by participants during the treatment period. Baseline assessments in this OLE study are defined by and taken directly from the Baseline assessments in the parent study NCT01336621.

End point type	Secondary

End point timeframe:

Baseline and up to 5.8 years

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[79]			
Units: Participants				
0 to <25 percent reduction	7			
25 to <50 percent reduction	13			
50 to <75 percent reduction	26			
75 to 100 percent reduction	42			

Notes:

[79] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in 28-day partial-onset seizure frequency

End point title	Percent change from Baseline in 28-day partial-onset seizure frequency

End point description:

The seizure frequency was recorded in daily seizure calendar by participants during the treatment period. Percent change from Baseline in 28-day partial onset seizure frequency was presented as mean and standard deviation (SD). Baseline assessments in this OLE study are defined by and taken directly from the Baseline assessments in the parent study NCT01336621. Percent change from Baseline was calculated as post-Baseline value minus Baseline value divided by Baseline value into 100.

End point type	Secondary

End point timeframe:

Baseline and up to 5.8 years

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[80]			
Units: Percent change				
arithmetic mean (standard deviation)				
Category title 1	-56.9 (± 52.46)			

Notes:

[80] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants experiencing an increase in 28-day partial-onset seizure frequency from Baseline

End point title	Number of participants experiencing an increase in 28-day partial-onset seizure frequency from Baseline

End point description:

The seizure frequency was recorded in daily seizure calendar by participants during the treatment period. Baseline assessments in this OLE study are defined by and taken directly from the Baseline assessments in the parent study NCT01336621.

End point type	Secondary

End point timeframe:

Baseline and up to 5.8 years

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[81]			
Units: Participants				
Participants	10			

Notes:

[81] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who remained seizure-free

End point title	Number of participants who remained seizure-free

End point description:

The seizure frequency was recorded in daily seizure calendar by participants during the treatment period. Number of participants who were treated retigabine for at least 6 months and who remained seizure free for any 6 continuous months as well as number of participants who were treated with retigabine for at least 12 months and who remained seizure free for any 12 continuous months are presented.

End point type	Secondary

End point timeframe:

Up to 5.8 years

End point values	Retigabine IR			
Subject group type	Reporting group			
Number of subjects analysed	98[82]			
Units: Participants				
Seizure free for 6 months; n= 85	27			
Seizure free for 12 months; n= 71	13			

Notes:

[82] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of the study treatment until the end of study treatment (up to 5.8 years).

Adverse event reporting additional description:

AEs and SAEs were collected in 'Safety Population' for retigabine IR arm and in 'All SFUCP subjects Population' for Retigabine IR in SFUCP arm. The MedDRA version for the Primary Reporting Phase is 19.1. However the SFUCP phase uses version 20.1.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Retigabine IR in SFUCP

Reporting group description:

Participants who withdrew from the Open-Label Treatment Phase and who had retinal pigmentation or unexplained vision loss, pigmentation of non-retinal ocular tissue or abnormal discoloration of nails, lips, skin or mucosa were followed-up in SFUCP following discontinuation of their retigabine, which was the final reporting phase of the study. During SFUCP, participants underwent six monthly comprehensive eye examinations and/or dermatological assessments. Participants were followed-up until the discoloration /pigmentation either resolves or stabilizes, as defined by no change over two consecutive six monthly assessments over at least 12 months after discontinuation of RTG IR .

Reporting group title	Retigabine IR

Reporting group description:

Eligible participants continued on the same maintenance dose of retigabine IR and the concurrent anti-epileptic drugs (AEDs) as they were taking at Visit 7 (Week 20) in the parent study NCT01336621. After the first week of the study, the dose of retigabine IR could be increased or decreased by 50-150 milligrams per day (mg/day) on a weekly basis. The overall daily dose of retigabine IR was to be maintained between 300 mg/day (minimum) and 1200 mg/day (maximum).

Serious adverse events	Retigabine IR in SFUCP	Retigabine IR	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	4 / 98 (4.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Hemoglobin decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma stage II			

subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Scar			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic psychosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Retigabine IR in SFUCP	Retigabine IR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	38 / 98 (38.78%)	
Investigations			
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	7 / 98 (7.14%)	
occurrences (all)	0	7	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast fibroma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	14 / 98 (14.29%)	
occurrences (all)	0	18	
Headache			
subjects affected / exposed	0 / 9 (0.00%)	10 / 98 (10.20%)	
occurrences (all)	0	23	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	11 / 98 (11.22%)	
occurrences (all)	0	20	
Eye disorders			
Iridocyclitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Oral mucosal discolouration			

subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	0 / 9 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	7	
Rhinitis allergic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Nail pigmentation			
subjects affected / exposed	0 / 9 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	6	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bacteriuria			
subjects affected / exposed	0 / 9 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	7	
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2013	To update the Sponsor Information page including change in Medical Monitor; to add the requirement to re-evaluate all ongoing participants at each clinic visit with respect to the risk versus the benefit of continuing treatment with Retigabine; revision of study conclusion conditions under which participants will continue to receive retigabine treatment; to re-consent all ongoing participants with revised patient information materials detailing the risk of retinal pigmentation, possible vision loss, pigmentation of non retinal ocular tissue, and discolouration of skin, lips, nails or Mucosa; Addition of 6-monthly comprehensive eye assessments by an ophthalmologist/retina specialist to assess for retinal pigmentation and/or unexplained vision loss; Addition of a skin examination by the investigator at scheduled clinic visits; Addition of referral to a dermatologist for abnormal skin discolouration noted by the investigator or reported by the participant, and repeat 6-monthly assessments by the dermatologist for follow-up of confirmed abnormal skin discolouration; Addition of a Safety Follow-Up / Continuation Phase to provide follow-up of participants who are found to have retinal pigmentation, unexplained vision loss, pigmentation of non-retinal ocular tissue or abnormal discolouration of skin, lips, nails or mucosa and who have stopped taking retigabine; Addition of safety endpoints related to abnormal pigmentation of the eye and/or discolouration of the skin, lips, nails or mucosa; Addition of Pharmacogenetics (PGx) sample collection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

17 parts. withdrew due to AE, however only 16 had a TEAE leading to withdrawal of RTG. 1 part. with a TEAE of seizure, withdrew due to lack of efficacy. 2 further parts. withdrew due to AE but had no TEAEs which led to withdrawal of RTG.

Notes: