



Clinical trial results:

A multicenter, open-label, long-term, safety, tolerability and efficacy study of retigabine in adult epilepsy patients with partial-onset seizures (Extension of Study VRX-RET-E22-302)

Summary

EudraCT number	2006-000956-42
Trial protocol	GB HU BE ES DE
Global end of trial date	

Results information

Result version number	v3
This version publication date	24 June 2018
First version publication date	08 April 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	VRX-RET-E22-304
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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	Interim
Date of interim/final analysis	25 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2017
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial: To evaluate the safety and tolerability of long-term therapy with retigabine administered as adjunctive therapy in adult epilepsy participants with partial-onset seizures, who completed the double-blind Study VRX-RET-E22-302

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	11 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Poland: 70
Country: Number of subjects enrolled	Russian Federation: 48
Country: Number of subjects enrolled	South Africa: 43
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Ukraine: 45
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	376
EEA total number of subjects	183

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	374
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multi-center, open-label, long-term, safety, tolerability and efficacy study involving 57 study sites in 13 countries (Australia, Belgium, France, Germany, Hungary, Israel, Poland, Russia, South Africa, Spain, Ukraine, the United Kingdom and the United States).

Pre-assignment

Screening details:

A total of 376 adult epilepsy participants with partial-onset seizures who completed the parent study (VRX-RET-E22-302 [NCT00235755]) entered this open label extension (OLE) study. The results presented are based on the analysis of data of primary reporting phase.

Period 1

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

Arms

Arm title	Retigabine
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Arm description:

Eligible participants entered a 4-week transition phase of the double-blind parent study (study VRX-RET-E22-302), in which their dose of retigabine was titrated to or maintained at 300 milligrams (mg) three times daily (900 mg per day). Upon completion of the Transition phase of the parent study, participants enrolled into the extension study (RTG115097). Once enrolled in the OLE, doses were adjusted within the range of 600 mg to 1200 mg per day as an adjunct therapy to their ongoing antiepileptic drugs (AEDs) with or without vagal nerve stimulation (VNS) up to 121 months.

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

Dosage and administration details:

Retigabine was supplied as 50, 100 and 300 mg film coated tablets. Participants received retigabine dose of 300 mg three times daily (900 mg per day) a 4-week transition phase. Once enrolled in the OLE, doses were adjusted within the range of 600 mg to 1200 mg per day as an adjunct therapy to their ongoing AEDs with or without VNS up to 120 months.

Number of subjects in period 1	Retigabine
Started	376
Completed	30
Not completed	346
Adverse event, serious fatal	5
Physician decision	2
Request of the sponsor	19
Due to pigmentation risk concerns	2

Persistent ALT/AST above 3 times the ULN	3
Participant request	2
Termination of study at sponsor request	3
Discontinuation of study	1
Missing	1
ALT/AST levels above 5 times the ULN	3
Consent withdrawn by subject	97
Change in participant medical condition	3
Ongoing SAE from parent study	1
Participant passed away	1
Failed to return	8
Adverse event, non-fatal	96
Participant request unrelated to study	2
Pregnancy	3
Ministry of Health decision	25
Participant Immigrated to New Zealand	1
Unknown	1
Participant retired the informed consent	1
Lack of efficacy	56
Protocol deviation	10

Baseline characteristics

Reporting groups

Reporting group title	Retigabine
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Reporting group description:

Eligible participants entered a 4-week transition phase of the double-blind parent study (study VRX-RET-E22-302), in which their dose of retigabine was titrated to or maintained at 300 milligrams (mg) three times daily (900 mg per day). Upon completion of the Transition phase of the parent study, participants enrolled into the extension study (RTG115097). Once enrolled in the OLE, doses were adjusted within the range of 600 mg to 1200 mg per day as an adjunct therapy to their ongoing antiepileptic drugs (AEDs) with or without vagal nerve stimulation (VNS) up to 121 months.

Reporting group values	Retigabine	Total	
Number of subjects	376	376	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	37.0 ± 11.85	-	
Gender categorical Units: Subjects			
Female	195	195	
Male	181	181	
Race/Ethnicity, Customized Units: Subjects			
Caucasian	360	360	
African-American (Black)	3	3	
Asian	3	3	
Unknown	10	10	

End points

End points reporting groups

Reporting group title	Retigabine
Reporting group description:	
Eligible participants entered a 4-week transition phase of the double-blind parent study (study VRX-RET-E22-302), in which their dose of retigabine was titrated to or maintained at 300 milligrams (mg) three times daily (900 mg per day). Upon completion of the Transition phase of the parent study, participants enrolled into the extension study (RTG115097). Once enrolled in the OLE, doses were adjusted within the range of 600 mg to 1200 mg per day as an adjunct therapy to their ongoing antiepileptic drugs (AEDs) with or without vagal nerve stimulation (VNS) up to 121 months.	

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

End point title	Number of participants with treatment emergent adverse events (TEAEs) and Serious adverse events (TESAEs) ^[1]
End point description:	
An AE is defined as 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/incapacity, is a congenital anomaly/birth defect, other situations and is associated with impaired liver function. TEAEs refer to an AE for which the onset was on or after 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 worsened in this study were also considered as TEAEs. Analysis was performed on the safety population which included participants who took at least 1 dose of study medication after being enrolled in this OLE study.	
End point type	Primary
End point timeframe:	
Up to 122 months	
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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[2]			
Units: Participants				
Any TEAE	324			
Any TESAE	78			

Notes:

[2] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with TEAEs leading to treatment discontinuation (disc.)

End point title	Number of participants with TEAEs leading to treatment discontinuation (disc.) ^[3]
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End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. A summary of participants with treatment emergent AEs leading to treatment disc. up to 122 months have been presented.

End point type	Primary
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End point timeframe:

Up to 122 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[4]			
Units: Participants				
Participants	115			

Notes:

[4] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier estimate of the Probability of disc. from Study Drug

End point title	Kaplan-Meier estimate of the Probability of disc. from Study Drug ^[5]
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End point description:

Kaplan-Meier estimate of the probability of disc. at the specified time for all participants is presented. The time frame of premature study disc. was defined as the time from the day of first the study medication to the time of withdrawal from study drug. For those who had a taper dose start date, the time of withdrawal was the day before the start of taper dose. Participants who switched to commercial product were censored at the last dose of study drug (excluding taper). All participants who withdrew from the study/treatment prematurely but did not switch to commercial product were counted as an event. Number of participants continuing on retigabine at each time of withdrawal were analyzed (represented by n=x in the category titles).

End point type	Primary
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End point timeframe:

Up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[6]			
Units: Percentage Probability of disc.				
number (not applicable)				
Day 0, n=374	0.5			
Day 1, n=371	1.3			
Day 2, n=369	1.9			

Day 3, n=368	2.1			
Day 4, n=367	2.4			
Day 5, n=366	2.7			
Day 6, n=365	2.9			
Day 11, n=364	3.2			
Day 13, n=363	3.5			
Day 14, n=362	3.7			
Day 16, n=361	4.0			
Day 21, n=360	4.3			
Day 22, n=359	4.5			
Day 27, n=356	5.3			
Day 28, n=350	6.9			
Day 29, n=348	7.4			
Day 30, n=344	8.5			
Day 32, n=343	8.8			
Day 35, n=341	9.3			
Day 40, n=340	9.6			
Day 41, n=339	9.8			
Day 42, n=338	10.1			
Day 45, n=337	10.4			
Day 50, n=336	10.6			
Day 56, n=335	10.9			
Day 61, n=334	11.2			
Day 62, n=333	11.4			
Day 63, n=331	12.0			
Day 71, n=330	12.2			
Day 77, n=329	12.5			
Day 82, n=328	12.8			
Day 85, n=326	13.3			
Day 86, n=325	13.6			
Day 88, n=324	13.8			
Day 90, n=322	14.4			
Day 91, n=316	16.0			
Day 92, n=313	16.8			
Day 94, n=312	17.0			
Day 95, n=310	17.6			
Day 99, n=309	17.8			
Day 104, n=308	18.1			
Day 105, n=307	18.4			
Day 107, n=306	18.6			
Day 110, n=305	18.9			
Day 112, n=303	19.4			
Day 118, n=302	19.7			
Day 121, n=300	20.2			
Day 122, n=299	20.5			
Day 126, n=298	20.7			
Day 132, n=297	21.0			
Day 134, n=296	21.3			
Day 135, n=295	21.5			
Day 138, n=294	21.8			
Day 139, n=293	22.1			
Day 141, n=292	22.3			

Day 152, n=291	22.6			
Day 155, n=290	22.9			
Day 161, n=289	23.1			
Day 164, n=288	23.4			
Day 172, n=287	23.7			
Day 176, n=286	23.9			
Day 179, n=282	25.0			
Day 180, n=278	26.1			
Day 181, n=275	26.9			
Day 182, n=273	27.4			
Day 183, n=272	27.7			
Day 184, n=271	27.9			
Day 187, n=270	28.2			
Day 188, n=269	28.5			
Day 189, n=268	28.7			
Day 192, n=267	29.0			
Day 195, n=265	29.5			
Day 198, n=264	29.8			
Day 199, n=263	30.1			
Day 204, n=262	30.3			
Day 214, n=261	30.6			
Day 216, n=260	30.9			
Day 218, n=259	31.1			
Day 221, n=258	31.4			
Day 228, n=257	31.6			
Day 231, n=256	31.9			
Day 233, n=255	32.2			
Day 235, n=254	32.4			
Day 236, n=253	32.7			
Day 237, n=251	33.2			
Day 252, n=250	33.5			
Day 260, n=249	33.8			
Day 264, n=248	34.0			
Day 265, n=247	34.3			
Day 269, n=246	34.6			
Day 270, n=245	34.8			
Day 272, n=240	36.2			
Day 274, n=239	36.4			
Day 275, n=238	36.7			
Day 276, n=236	37.2			
Day 278, n=235	37.5			
Day 279, n=234	37.8			
Day 292, n=233	38.0			
Day 299, n=231	38.6			
Day 301, n=230	38.8			
Day 310, n=229	39.1			
Day 315, n=228	39.4			
Day 316, n=227	39.6			
Day 317, n=226	39.9			
Day 322, n=225	40.2			
Day 325, n=224	40.4			
Day 339, n=223	40.7			

Day 351, n=222	41.0			
Day 357, n=221	41.2			
Day 358, n=219	41.8			
Day 363, n=218	42.0			
Day 372, n=217	42.3			
Day 375, n=216	42.6			
Day 377, n=215	42.8			
Day 416, n=214	43.1			
Day 419, n=213	43.4			
Day 425, n=212	43.6			
Day 429, n=211	43.9			
Day 437, n=210	44.1			
Day 447, n=209	44.4			
Day 455, n=208	44.7			
Day 458, n=207	44.9			
Day 460, n=206	45.2			
Day 461, n=205	45.5			
Day 478, n=204	45.7			
Day 480, n=203	46.0			
Day 482, n=202	46.3			
Day 485, n=200	46.8			
Day 492, n=197	47.6			
Day 493, n=196	47.9			
Day 497, n=194	48.4			
Day 498, n=193	48.7			
Day 501, n=192	48.9			
Day 523, n=191	49.2			
Day 525, n=190	49.5			
Day 534, n=189	49.7			
Day 536, n=188	50.0			
Day 541, n=187	50.3			
Day 553, n=186	50.5			
Day 556, n=185	50.8			
Day 587, n=184	51.1			
Day 593, n=183	51.3			
Day 594, n=182	51.6			
Day 596, n=181	51.9			
Day 601, n=180	52.1			
Day 602, n=178	52.7			
Day 610, n=177	52.9			
Day 612, n=176	53.2			
Day 617, n=175	53.5			
Day 618, n=174	53.7			
Day 632, n=173	54.0			
Day 635, n=172	54.3			
Day 669, n=171	54.5			
Day 676, n=170	54.8			
Day 678, n=169	55.1			
Day 685, n=168	55.3			
Day 700, n=167	55.6			
Day 702, n=165	56.1			
Day 703, n=164	56.4			

Day 707, n=163	56.6			
Day 714, n=162	56.9			
Day 719, n=161	57.2			
Day 720, n=160	57.4			
Day 721, n=159	57.7			
Day 724, n=158	58.0			
Day 729, n=157	58.2			
Day 760, n=156	58.5			
Day 775, n=155	58.8			
Day 777, n=154	59.0			
Day 778, n=153	59.3			
Day 779, n=152	59.6			
Day 781, n=151	59.8			
Day 796, n=150	60.1			
Day 803, n=149	60.4			
Day 818, n=148	60.6			
Day 835, n=147	60.9			
Day 840, n=146	61.2			
Day 841, n=144	61.7			
Day 842, n=143	62.0			
Day 844, n=142	62.2			
Day 845, n=141	62.5			
Day 855, n=140	62.8			
Day 856, n=139	63.0			
Day 863, n=138	63.3			
Day 870, n=137	63.6			
Day 884, n=136	63.8			
Day 893, n=135	64.1			
Day 904, n=134	64.4			
Day 924, n=133	64.6			
Day 927, n=132	64.9			
Day 938, n=131	65.2			
Day 944, n=130	65.4			
Day 947, n=128	66.0			
Day 952, n=127	66.2			
Day 975, n=126	66.5			
Day 980, n=125	66.8			
Day 994, n=123	67.3			
Day 1067, n=122	67.6			
Day 1074, n=121	67.8			
Day 1084, n=120	68.1			
Day 1091, n=119	68.4			
Day 1129, n=118	68.6			
Day 1141, n=117	68.9			
Day 1142, n=116	69.1			
Day 1148, n=115	69.4			
Day 1196, n=114	69.7			
Day 1198, n=113	69.9			
Day 1206, n=112	70.2			
Day 1207, n=111	70.5			
Day 1211, n=110	70.7			
Day 1221, n=109	71.0			

Day 1231, n=108	71.3			
Day 1299, n=107	71.5			
Day 1316, n=106	71.8			
Day 1322, n=105	72.1			
Day 1389, n=104	72.3			
Day 1413, n=103	72.6			
Day 1436, n=102	72.6			
Day 1446, n=101	72.9			
Day 1450, n=100	73.1			
Day 1451, n=99	73.1			
Day 1452, n=98	73.4			
Day 1521, n=97	73.7			
Day 1541, n=96	73.7			
Day 1545, n=95	73.7			
Day 1547, n=94	74.0			
Day 1563, n=93	74.0			
Day 1567, n=92	74.2			
Day 1569, n=91	74.5			
Day 1589, n=90	74.5			
Day 1618, n=89	74.5			
Day 1619, n=88	74.5			
Day 1623, n=87	74.5			
Day 1632, n=86	74.5			
Day 1656, n=85	74.5			
Day 1660, n=84	74.5			
Day 1668, n=83	74.8			
Day 1672, n=82	75.1			
Day 1676, n=81	75.4			
Day 1680, n=80	75.4			
Day 1694, n=79	75.4			
Day 1697, n=78	75.4			
Day 1752, n=77	75.4			
Day 1756, n=76	75.8			
Day 1760, n=75	75.8			
Day 1792, n=74	76.1			
Day 1802, n=73	76.1			
Day 1807, n=72	76.1			
Day 1814, n=71	76.4			
Day 1819, n=70	76.4			
Day 1836, n=69	76.4			
Day 1849, n=68	76.4			
Day 1855, n=67	76.4			
Day 1887, n=66	76.4			
Day 1895, n=65	76.8			
Day 1904, n=64	76.8			
Day 1919, n=63	76.8			
Day 1920, n=62	77.1			
Day 1926, n=61	77.5			
Day 1928, n=60	77.5			
Day 1929, n=59	77.9			
Day 1931, n=58	78.3			
Day 1937, n=57	78.3			

Day 1951, n=56	78.6			
Day 2005, n=55	79.0			
Day 2037, n=54	79.4			
Day 2044, n=53	79.4			
Day 2092, n=52	79.8			
Day 2157, n=51	80.2			
Day 2161, n=50	80.6			
Day 2162, n=49	81.0			
Day 2182, n=48	81.3			
Day 2183, n=47	81.7			
Day 2184, n=46	82.1			
Day 2227, n=45	82.5			
Day 2281, n=44	82.9			
Day 2283, n=43	83.3			
Day 2285, n=42	83.7			
Day 2296, n=41	83.7			
Day 2317, n=40	84.1			
Day 2380, n=39	84.5			
Day 2395, n=37	85.3			
Day 2400, n=36	85.7			
Day 2405, n=35	86.1			
Day 2408, n=34	86.5			
Day 2415, n=33	86.9			
Day 2443, n=32	86.9			
Day 2525, n=31	87.3			
Day 2533, n=30	87.7			
Day 2537, n=29	88.1			
Day 2639, n=28	88.5			
Day 2664, n=27	88.9			
Day 2772, n=26	89.3			
Day 2793, n=25	89.7			
Day 2829, n=24	90.1			
Day 2870, n=23	90.6			
Day 2884, n=22	91.0			
Day 2973, n=21	91.4			
Day 2975, n=20	91.8			
Day 2998, n=19	92.2			
Day 3101, n=18	92.6			
Day 3118, n=17	93.0			
Day 3137, n=16	93.4			
Day 3144, n=15	93.8			
Day 3147, n=14	94.3			
Day 3185, n=13	94.7			
Day 3220, n=11	95.5			
Day 3231, n=10	95.9			
Day 3243, n=9	96.3			
Day 3246, n=8	96.7			
Day 3276, n=7	97.1			
Day 3277, n=6	97.5			
Day 3285, n=5	97.9			
Day 3318, n=4	98.4			
Day 3360, n=3	98.8			

Day 3483, n=2	99.2			
Day 3582, n=1	99.6			

Notes:

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements in the supine and standing position

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements in the supine and standing position ^[7]
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End point description:

Vital sign measurements (supine and standing blood pressure) were obtained throughout the study at all visits during the Open-Label Treatment Phase of the study. Evaluations of blood pressure were performed supine at each study visit, and again after the participant had been standing for approximately 2 minutes. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[8]			
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
Supine DBP, Visit 1 (Month 1), n=358	0.4 (± 10.05)			
Supine DBP, Visit 2 (Month 3), n=328	0.3 (± 9.83)			
Supine DBP, Visit 3 (Month 6), n=287	-0.2 (± 10.19)			
Supine DBP, Visit 4 (Month 9), n=251	0.0 (± 11.09)			
Supine DBP, Visit 5 (Month 12), n=235	0.7 (± 10.79)			
Supine DBP, Visit 6 (Month 16), n=202	1.0 (± 10.02)			
Supine DBP, Visit 7 (Month 20), n=181	0.4 (± 10.03)			
Supine DBP, Visit 8 (Month 24), n=167	0.4 (± 10.63)			
Supine DBP, Visit 9 (Month 28), n=147	1.5 (± 10.62)			
Supine DBP, Visit 10 (Month 32), n=128	0.0 (± 10.42)			
Supine DBP, Visit 11 (Month 36), n=121	1.0 (± 10.65)			
Supine DBP, Visit 12 (Month 40), n=112	2.0 (± 10.37)			
Supine DBP, Visit 13 (Month 44), n=105	0.5 (± 9.54)			
Supine DBP, Visit 14 (Month 48), n=104	0.0 (± 10.30)			
Supine DBP, Visit 15 (Month 52), n=91	0.1 (± 11.10)			
Supine DBP, Visit 16 (Month 56), n=77	1.2 (± 9.68)			
Supine DBP, Visit 17 (Month 60), n=92	-1.0 (± 11.08)			

Supine DBP, Visit 18 (Month 64), n=58	1.6 (± 8.29)			
Supine DBP, Visit 19 (Month 68), n=53	0.6 (± 8.66)			
Supine DBP, Visit 20 (Month 72), n=61	1.3 (± 8.38)			
Supine DBP, Visit 21 (Month 76), n=43	3.2 (± 8.88)			
Supine DBP, Visit 22 (Month 80), n=37	1.8 (± 7.66)			
Supine DBP, Visit 23 (Month 84), n=32	-1.4 (± 8.64)			
Supine DBP, Visit 24 (Month 88), n=29	3.4 (± 8.83)			
Supine DBP, Visit 25 (Month 92), n=25	2.3 (± 7.29)			
Supine DBP, Visit 26 (Month 96), n=26	1.5 (± 10.10)			
Supine DBP, Visit 27 (Month 100), n=20	1.5 (± 8.42)			
Supine DBP, Visit 28 (Month 104), n=17	3.4 (± 10.56)			
Supine DBP, Visit 29 (Month 108), n=13	0.5 (± 6.74)			
Supine DBP, Visit 30 (Month 112), n=4	4.0 (± 7.30)			
Supine DBP, Visit 31 (Month 116), n=3	11.0 (± 7.55)			
Supine DBP, Visit 32 (Month 120), n=1	-2.0 (± 99999)			
Supine DBP, Follow up, n=267	1.3 (± 10.08)			
Standing DBP, Visit 1 (Month 1), n=357	0.6 (± 10.68)			
Standing DBP, Visit 2 (Month 3), n=328	0.2 (± 10.62)			
Standing DBP, Visit 3 (Month 6), n=287	-0.1 (± 10.21)			
Standing DBP, Visit 4 (Month 9), n=251	0.2 (± 10.14)			
Standing DBP, Visit 5 (Month 12), n=235	0.8 (± 10.17)			
Standing DBP, Visit 6 (Month 16), n=202	0.3 (± 10.16)			
Standing DBP, Visit 7 (Month 20), n=181	0.4 (± 9.51)			
Standing DBP, Visit 8 (Month 24), n=167	0.2 (± 9.83)			
Standing DBP, Visit 9 (Month 28), n=147	0.3 (± 10.00)			
Standing DBP, Visit 10 (Month 32), n=128	-0.6 (± 10.64)			
Standing DBP, Visit 11 (Month 36), n=121	0.9 (± 10.94)			
Standing DBP, Visit 12 (Month 40), n=111	1.4 (± 11.01)			
Standing DBP, Visit 13 (Month 44), n=105	-0.2 (± 10.76)			
Standing DBP, Visit 14 (Month 48), n=104	0.3 (± 10.35)			
Standing DBP, Visit 15 (Month 52), n=91	-1.5 (± 11.00)			
Standing DBP, Visit 16 (Month 56), n=77	-0.3 (± 10.40)			
Standing DBP, Visit 17 (Month 60), n=92	-1.5 (± 9.70)			
Standing DBP, Visit 18 (Month 64), n=58	0.5 (± 8.07)			
Standing DBP, Visit 19 (Month 68), n=53	0.0 (± 7.20)			
Standing DBP, Visit 20 (Month 72), n=61	0.3 (± 8.31)			
Standing DBP, Visit 21 (Month 76), n=43	1.4 (± 8.93)			
Standing DBP, Visit 22 (Month 80), n=37	0.3 (± 8.03)			
Standing DBP, Visit 23 (Month 84), n=32	-0.4 (± 7.98)			

Standing DBP, Visit 24 (Month 88), n=29	1.6 (± 8.38)			
Standing DBP, Visit 25 (Month 92), n=25	1.0 (± 7.33)			
Standing DBP, Visit 26 (Month 96), n=26	1.6 (± 9.20)			
Standing DBP, Visit 27 (Month 100), n=20	0.2 (± 10.48)			
Standing DBP, Visit 28 (Month 104), n=17	2.8 (± 11.65)			
Standing DBP, Visit 29 (Month 108), n=13	-0.5 (± 9.42)			
Standing DBP, Visit 30 (Month 112), n=4	1.3 (± 9.18)			
Standing DBP, Visit 31 (Month 116), n=3	8.0 (± 11.79)			
Standing DBP, Visit 32 (Month 120), n=1	-1.0 (± 99999)			
Standing DBP, Follow up, n=267	2.0 (± 10.57)			
Supine SBP, Visit 1 (Month 1), n=358	-0.2 (± 12.03)			
Supine SBP, Visit 2 (Month 3), n=328	-0.4 (± 12.09)			
Supine SBP, Visit 3 (Month 6), n=287	0.5 (± 13.53)			
Supine SBP, Visit 4 (Month 9), n=251	0.0 (± 15.32)			
Supine SBP, Visit 5 (Month 12), n=235	0.5 (± 12.99)			
Supine SBP, Visit 6 (Month 16), n=202	0.7 (± 14.39)			
Supine SBP, Visit 7 (Month 20), n=181	-0.5 (± 14.34)			
Supine SBP, Visit 8 (Month 24), n=167	-0.4 (± 14.11)			
Supine SBP, Visit 9 (Month 28), n=147	0.2 (± 13.78)			
Supine SBP, Visit 10 (Month 32), n=128	0.3 (± 13.60)			
Supine SBP, Visit 11 (Month 36), n=121	0.2 (± 14.90)			
Supine SBP, Visit 12 (Month 40), n=112	1.3 (± 13.90)			
Supine SBP, Visit 13 (Month 44), n=105	0.1 (± 11.28)			
Supine SBP, Visit 14 (Month 48), n=104	-1.1 (± 13.03)			
Supine SBP, Visit 15 (Month 52), n=91	-0.7 (± 14.05)			
Supine SBP, Visit 16 (Month 56), n=77	2.6 (± 13.41)			
Supine SBP, Visit 17 (Month 60), n=92	-0.2 (± 14.48)			
Supine SBP, Visit 18 (Month 64), n=58	1.8 (± 12.11)			
Supine SBP, Visit 19 (Month 68), n=53	1.1 (± 13.00)			
Supine SBP, Visit 20 (Month 72), n=61	2.5 (± 10.26)			
Supine SBP, Visit 21 (Month 76), n=43	4.4 (± 15.51)			
Supine SBP, Visit 22 (Month 80), n=37	2.3 (± 15.13)			
Supine SBP, Visit 23 (Month 84), n=32	1.1 (± 13.90)			
Supine SBP, Visit 24 (Month 88), n=29	2.7 (± 12.51)			
Supine SBP, Visit 25 (Month 92), n=25	2.8 (± 10.44)			
Supine SBP, Visit 26 (Month 96), n=26	2.9 (± 14.66)			
Supine SBP, Visit 27 (Month 100), n=20	2.6 (± 10.61)			
Supine SBP, Visit 28 (Month 104), n=17	5.8 (± 10.91)			
Supine SBP, Visit 29 (Month 108), n=13	-2.2 (± 8.68)			
Supine SBP, Visit 30 (Month 112), n=4	8.5 (± 6.95)			
Supine SBP, Visit 31 (Month 116), n=3	13.7 (± 4.93)			
Supine SBP, Visit 32 (Month 120), n=1	11.0 (± 99999)			
Supine SBP, Follow up, n=267	1.2 (± 14.15)			
Standing SBP, Visit 1 (Month 1), n=357	-1.2 (± 12.20)			
Standing SBP, Visit 2 (Month 3), n=328	-0.7 (± 13.30)			
Standing SBP, Visit 3 (Month 6), n=287	-0.2 (± 13.89)			

Standing SBP, Visit 4 (Month 9), n=251	-0.7 (± 15.10)			
Standing SBP, Visit 5 (Month 12), n=235	-0.7 (± 14.56)			
Standing SBP, Visit 6 (Month 16), n=202	-0.3 (± 14.09)			
Standing SBP, Visit 7 (Month 20), n=181	-0.8 (± 15.19)			
Standing SBP, Visit 8 (Month 24), n=167	-0.5 (± 15.35)			
Standing SBP, Visit 9 (Month 28), n=147	-0.3 (± 16.30)			
Standing SBP, Visit 10 (Month 32), n=128	-0.1 (± 15.06)			
Standing SBP, Visit 11 (Month 36), n=121	0.7 (± 15.51)			
Standing SBP, Visit 12 (Month 40), n=111	2.7 (± 14.21)			
Standing SBP, Visit 13 (Month 44), n=105	-1.3 (± 12.57)			
Standing SBP, Visit 14 (Month 48), n=104	-1.6 (± 14.67)			
Standing SBP, Visit 15 (Month 52), n=91	-1.2 (± 14.35)			
Standing SBP, Visit 16 (Month 56), n=77	0.9 (± 15.04)			
Standing SBP, Visit 17 (Month 60), n=92	-0.7 (± 14.92)			
Standing SBP, Visit 18 (Month 64), n=58	0.6 (± 12.84)			
Standing SBP, Visit 19 (Month 68), n=53	0.2 (± 11.85)			
Standing SBP, Visit 20 (Month 72), n=61	0.5 (± 12.43)			
Standing SBP, Visit 21 (Month 76), n=43	3.5 (± 12.47)			
Standing SBP, Visit 22 (Month 80), n=37	0.9 (± 14.31)			
Standing SBP, Visit 23 (Month 84), n=32	-0.8 (± 14.85)			
Standing SBP, Visit 24 (Month 88), n=29	-0.6 (± 13.28)			
Standing SBP, Visit 25 (Month 92), n=25	-1.6 (± 10.49)			
Standing SBP, Visit 26 (Month 96), n=26	-0.2 (± 14.68)			
Standing SBP, Visit 27 (Month 100), n=20	0.0 (± 12.62)			
Standing SBP, Visit 28 (Month 104), n=17	2.9 (± 11.70)			
Standing SBP, Visit 29 (Month 108), n=13	-2.2 (± 10.58)			
Standing SBP, Visit 30 (Month 112), n=4	1.8 (± 9.60)			
Standing SBP, Visit 31 (Month 116), n=3	9.0 (± 1.00)			
Standing SBP, Visit 32 (Month 120), n=1	10.0 (± 99999)			
Standing SBP, Follow up, n=267	1.4 (± 14.59)			

Notes:

[8] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in heart rate (HR) measurements in the supine and standing position

End point title	Change from Baseline in heart rate (HR) measurements in the supine and standing position ^[9]
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End point description:

Vital sign measurement HR was obtained throughout the study at all visits during the Open-Label Treatment Phase of the study. Evaluations of HR was performed supine at each study visit, and again after the participant had been standing for approximately 2 minutes. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[10]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Supine HR, Visit 1 (Month 1), n=358	-0.4 (± 9.89)			
Supine HR, Visit 2 (Month 3), n=328	-0.5 (± 9.93)			
Supine HR, Visit 3 (Month 6), n=287	0.1 (± 9.62)			
Supine HR, Visit 4 (Month 9), n=252	0.7 (± 9.69)			
Supine HR, Visit 5 (Month 12), n=235	0.0 (± 9.83)			
Supine HR, Visit 6 (Month 16), n=202	1.8 (± 10.56)			
Supine HR, Visit 7 (Month 20), n=181	2.3 (± 11.87)			
Supine HR, Visit 8 (Month 24), n=167	1.9 (± 10.28)			
Supine HR, Visit 9 (Month 28), n=147	2.7 (± 10.86)			
Supine HR, Visit 10 (Month 32), n=128	3.0 (± 10.50)			
Supine HR, Visit 11 (Month 36), n=121	0.8 (± 10.33)			
Supine HR, Visit 12 (Month 40), n=112	3.3 (± 11.20)			
Supine HR, Visit 13 (Month 44), n=105	1.8 (± 10.59)			
Supine HR, Visit 14 (Month 48), n=104	1.0 (± 10.78)			
Supine HR, Visit 15 (Month 52), n=91	2.0 (± 12.20)			
Supine HR, Visit 16 (Month 56), n=77	2.5 (± 10.70)			
Supine HR, Visit 17 (Month 60), n=92	0.9 (± 12.25)			
Supine HR, Visit 18 (Month 64), n=58	5.5 (± 10.44)			

Supine HR, Visit 19 (Month 68), n=53	2.4 (± 10.19)			
Supine HR, Visit 20 (Month 72), n=61	2.1 (± 12.23)			
Supine HR, Visit 21 (Month 76), n=43	2.8 (± 9.30)			
Supine HR, Visit 22 (Month 80), n=37	5.1 (± 10.13)			
Supine HR, Visit 23 (Month 84), n=32	3.5 (± 11.98)			
Supine HR, Visit 24 (Month 88), n=29	3.2 (± 13.66)			
Supine HR, Visit 25 (Month 92), n=25	3.9 (± 9.89)			
Supine HR, Visit 26 (Month 96), n=26	2.1 (± 10.37)			
Supine HR, Visit 27 (Month 100), n=20	3.1 (± 9.82)			
Supine HR, Visit 28 (Month 104), n=17	3.3 (± 8.62)			
Supine HR, Visit 29 (Month 108), n=13	0.5 (± 8.93)			
Supine HR, Visit 30 (Month 112), n=4	3.8 (± 12.84)			
Supine HR, Visit 31 (Month 116), n=3	7.7 (± 13.43)			
Supine HR, Visit 32 (Month 120), n=1	11.0 (± 99999)			
Supine HR, Follow up, n=267	2.1 (± 10.44)			
Standing HR, Visit 1 (Month 1), n=357	-0.1 (± 11.10)			
Standing HR, Visit 2 (Month 3), n=328	-0.2 (± 11.01)			
Standing HR, Visit 3 (Month 6), n=287	0.3 (± 10.39)			
Standing HR, Visit 4 (Month 9), n=252	1.7 (± 11.53)			
Standing HR, Visit 5 (Month 12), n=235	0.1 (± 11.06)			
Standing HR, Visit 6 (Month 16), n=202	1.6 (± 12.35)			
Standing HR, Visit 7 (Month 20), n=181	1.4 (± 12.71)			
Standing HR, Visit 8 (Month 24), n=167	1.9 (± 10.93)			
Standing HR, Visit 9 (Month 28), n=147	1.6 (± 11.25)			
Standing HR, Visit 10 (Month 32), n=128	2.2 (± 11.92)			
Standing HR, Visit 11 (Month 36), n=121	-0.6 (± 11.23)			
Standing HR, Visit 12 (Month 40), n=111	2.6 (± 12.94)			
Standing HR, Visit 13 (Month 44), n=105	2.8 (± 11.22)			
Standing HR, Visit 14 (Month 48), n=104	0.8 (± 11.81)			
Standing HR, Visit 15 (Month 52), n=91	3.1 (± 12.09)			
Standing HR, Visit 16 (Month 56), n=77	1.3 (± 12.12)			
Standing HR, Visit 17 (Month 60), n=92	0.6 (± 12.26)			
Standing HR, Visit 18 (Month 64), n=58	4.6 (± 12.09)			
Standing HR, Visit 19 (Month 68), n=52	1.3 (± 10.78)			
Standing HR, Visit 20 (Month 72), n=61	0.7 (± 13.45)			
Standing HR, Visit 21 (Month 76), n=43	0.3 (± 10.83)			
Standing HR, Visit 22 (Month 80), n=37	2.9 (± 10.96)			
Standing HR, Visit 23 (Month 84), n=32	2.3 (± 9.76)			
Standing HR, Visit 24 (Month 88), n=29	2.4 (± 10.64)			
Standing HR, Visit 25 (Month 92), n=25	3.6 (± 12.61)			
Standing HR, Visit 26 (Month 96), n=26	3.1 (± 12.01)			
Standing HR, Visit 27 (Month 100), n=20	5.2 (± 9.88)			
Standing HR, Visit 28 (Month 104), n=17	6.2 (± 11.00)			
Standing HR, Visit 29 (Month 108), n=13	-0.2 (± 8.94)			
Standing HR, Visit 30 (Month 112), n=4	2.3 (± 12.84)			
Standing HR, Visit 31 (Month 116), n=3	7.3 (± 12.10)			

Standing HR, Visit 32 (Month 120), n=1	10.0 ($\pm$ 99999)			
Standing HR, Follow up, n=267	2.2 ($\pm$ 11.39)			

Notes:

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body temperature

End point title	Change from Baseline in body temperature ^[11]
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End point description:

Vital sign measurement temperature was obtained throughout the study at all visits during the Open-Label Treatment Phase of the study. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[12]			
Units: Degree Celsius				
arithmetic mean (standard deviation)				
Body temperature, Visit 1 (Month 1), n=350	0.02 ($\pm$ 0.386)			
Body temperature, Visit 2 (Month 3), n=318	0.02 ($\pm$ 0.358)			
Body temperature, Visit 3 (Month 6), n=280	0.03 ($\pm$ 0.384)			
Body temperature, Visit 4 (Month 9), n=244	0.00 ($\pm$ 0.380)			
Body temperature, Visit 5 (Month 12), n=229	0.01 ($\pm$ 0.392)			
Body temperature, Visit 6 (Month 16), n=197	0.02 ($\pm$ 0.362)			
Body temperature, Visit 7 (Month 20), n=176	0.04 ($\pm$ 0.381)			
Body temperature, Visit 8 (Month 24), n=161	0.02 ($\pm$ 0.387)			
Body temperature, Visit 9 (Month 28), n=143	0.01 ($\pm$ 0.407)			
Body temperature, Visit 10 (Month 32), n=125	0.02 ($\pm$ 0.362)			
Body temperature, Visit 11 (Month 36), n=118	0.02 ($\pm$ 0.385)			
Body temperature, Visit 12 (Month 40), n=109	0.01 ($\pm$ 0.404)			

Body temperature, Visit 13 (Month 44), n=101	0.04 (± 0.387)			
Body temperature, Visit 14 (Month 48), n=100	0.05 (± 0.382)			
Body temperature, Visit 15 (Month 52), n=88	-0.02 (± 0.396)			
Body temperature, Visit 16 (Month 56), n=74	-0.01 (± 0.393)			
Body temperature, Visit 17 (Month 60), n=89	0.03 (± 0.391)			
Body temperature, Visit 18 (Month 64), n=58	-0.01 (± 0.306)			
Body temperature, Visit 19 (Month 68), n=53	0.05 (± 0.318)			
Body temperature, Visit 20 (Month 72), n=59	0.06 (± 0.373)			
Body temperature, Visit 21 (Month 76), n=42	0.06 (± 0.306)			
Body temperature, Visit 22 (Month 80), n=37	-0.04 (± 0.362)			
Body temperature, Visit 23 (Month 84), n=32	0.05 (± 0.324)			
Body temperature, Visit 24 (Month 88), n=29	-0.06 (± 0.313)			
Body temperature, Visit 25 (Month 92), n=25	0.00 (± 0.289)			
Body temperature, Visit 26 (Month 96), n=26	-0.10 (± 0.299)			
Body temperature, Visit 27 (Month 100), n=20	-0.03 (± 0.285)			
Body temperature, Visit 28 (Month 104), n=17	-0.02 (± 0.326)			
Body temperature, Visit 29 (Month 108), n=13	0.04 (± 0.275)			
Body temperature, Visit 30 (Month 112), n=4	-0.02 (± 0.126)			
Body temperature, Visit 31 (Month 116), n=3	-0.20 (± 0.200)			
Body temperature, Visit 32 (Month 120), n=1	0.10 (± 99999)			
Body temperature, Follow up, n=261	0.03 (± 0.397)			

Notes:

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body weight

End point title	Change from Baseline in body weight ^[13]
End point description:	
Weight in pounds or kilograms was measured in ordinary indoor clothing (without shoes) and was recorded at all study visits during the Open-Label Treatment Phase of the study. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).	
End point type	Primary

End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[14]			
Units: Kilograms				
arithmetic mean (standard deviation)				
Body weight, Visit 1 (Month 1), n=356	1.19 (± 3.125)			
Body weight, Visit 2 (Month 3), n=325	1.37 (± 3.630)			
Body weight, Visit 3 (Month 6), n=287	1.51 (± 4.528)			
Body weight, Visit 4 (Month 9), n=252	1.08 (± 5.068)			
Body weight, Visit 5 (Month 12), n=235	1.56 (± 4.764)			
Body weight, Visit 6 (Month 16), n=202	1.98 (± 5.382)			
Body weight, Visit 7 (Month 20), n=181	1.79 (± 5.762)			
Body weight, Visit 8 (Month 24), n=167	1.20 (± 6.571)			
Body weight, Visit 9 (Month 28), n=147	1.67 (± 6.101)			
Body weight, Visit 10 (Month 32), n=128	1.75 (± 7.103)			
Body weight, Visit 11 (Month 36), n=121	2.07 (± 7.151)			
Body weight, Visit 12 (Month 40), n=112	2.12 (± 7.077)			
Body weight, Visit 13 (Month 44), n=105	1.09 (± 7.469)			
Body weight, Visit 14 (Month 48), n=104	1.08 (± 8.007)			
Body weight, Visit 15 (Month 52), n=91	0.66 (± 7.539)			
Body weight, Visit 16 (Month 56), n=77	0.71 (± 7.248)			
Body weight, Visit 17 (Month 60), n=91	1.31 (± 8.082)			
Body weight, Visit 18 (Month 64), n=58	1.32 (± 7.541)			
Body weight, Visit 19 (Month 68), n=53	1.49 (± 8.036)			
Body weight, Visit 20 (Month 72), n=61	1.65 (± 8.774)			
Body weight, Visit 21 (Month 76), n=43	1.71 (± 9.355)			
Body weight, Visit 22 (Month 80), n=37	2.30 (± 9.311)			
Body weight, Visit 23 (Month 84), n=32	2.00 (± 9.522)			
Body weight, Visit 24 (Month 88), n=29	1.12 (± 9.633)			
Body weight, Visit 25 (Month 92), n=25	0.83 (± 10.845)			
Body weight, Visit 26 (Month 96), n=26	0.12 (± 14.470)			
Body weight, Visit 27 (Month 100), n=20	1.57 (± 11.382)			
Body weight, Visit 28 (Month 104), n=17	1.62 (± 10.715)			
Body weight, Visit 29 (Month 108), n=13	2.32 (± 13.914)			
Body weight, Visit 30 (Month 112), n=4	4.85 (± 17.693)			
Body weight, Visit 31 (Month 116), n=3	9.73 (± 17.234)			
Body weight, Visit 32 (Month 120), n=1	0.50 (± 99999)			

Body weight, Follow up, n=267	1.34 ($\pm$ 5.870)			
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Notes:

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Electrocardiogram (ECG) parameters PR, QRS, QT, corrected QT interval (QTc) Bazett and QTc Friedericia

End point title	Change from Baseline in Electrocardiogram (ECG) parameters PR, QRS, QT, corrected QT interval (QTc) Bazett and QTc Friedericia ^[15]
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End point description:

A 12-lead ECG was performed at all study visits during the Open-Label Treatment Phase during the first year of the open-label extension study (Months 1, 3, 6, 9, 12) and at the end of each 12 month study cycle that the participant was enrolled (i.e., second year, third year, fourth year, etc.). The ECG parameters that were assessed were PR interval, QRS interval, QRS duration, QT interval, and QTc interval. QT intervals were corrected using both Bazett's and Friedericia's formulas. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates data was not available. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[16]			
Units: Milliseconds				
arithmetic mean (standard deviation)				
PR interval, Visit 1 (Month 1), n=355	0.1 ($\pm$ 13.47)			
PR interval, Visit 2 (Month 3), n=324	-0.4 ($\pm$ 11.95)			
PR interval, Visit 3 (Month 6), n=278	-1.0 ($\pm$ 13.18)			
PR interval, Visit 4 (Month 9), n=245	-1.7 ($\pm$ 12.74)			
PR interval, Visit 5 (Month 12), n=233	-1.7 ($\pm$ 13.01)			
PR interval, Visit 8 (Month 24), n=158	-2.1 ($\pm$ 15.23)			
PR interval, Visit 11 (Month 36), n=113	-1.6 ($\pm$ 14.20)			
PR interval, Visit 14 (Month 48), n=98	0.3 ($\pm$ 13.30)			
PR interval, Visit 17 (Month 60), n=87	0.7 ($\pm$ 13.70)			
PR interval, Visit 20 (Month 72), n=52	0.9 ($\pm$ 14.07)			
PR interval, Visit 23 (Month 84), n=30	-3.5 ($\pm$ 13.06)			
PR interval, Visit 26 (Month 96), n=22	-4.4 ($\pm$ 11.96)			
PR interval, Visit 29 (Month 108), n=13	-1.9 ($\pm$ 11.50)			
PR interval, Visit 32 (Month 120), n=1	-23.7 ($\pm$ 99999)			
PR interval, Follow up, n=252	-1.3 ($\pm$ 12.83)			

QRS duration, Visit 1 (Month 1), n=357	-0.6 (± 8.03)			
QRS duration, Visit 2 (Month 3), n=327	-1.1 (± 7.53)			
QRS duration, Visit 3 (Month 6), n=282	-1.2 (± 7.34)			
QRS duration, Visit 4 (Month 9), n=249	-1.4 (± 6.59)			
QRS duration, Visit 5 (Month 12), n=235	-0.1 (± 8.09)			
QRS duration, Visit 8 (Month 24), n=160	-1.1 (± 7.74)			
QRS duration, Visit 11 (Month 36), n=116	1.5 (± 7.66)			
QRS duration, Visit 14 (Month 48), n=99	1.1 (± 7.92)			
QRS duration, Visit 17 (Month 60), n=89	3.3 (± 12.89)			
QRS duration, Visit 20 (Month 72), n=56	5.2 (± 16.42)			
QRS duration, Visit 23 (Month 84), n=32	3.4 (± 18.65)			
QRS duration Visit 26 (Month 96), n=23	3.5 (± 24.77)			
QRS duration, Visit 29 (Month 108), n=13	1.2 (± 7.73)			
QRS duration, Visit 32 (Month 120), n=1	10.7 (± 99999)			
QRS duration, Follow up, n=254	-0.1 (± 8.74)			
QT interval, Visit 1 (Month 1), n=357	5.5 (± 23.66)			
QT interval, Visit 2 (Month 3), n=324	4.8 (± 23.35)			
QT interval, Visit 3 (Month 6), n=278	5.3 (± 23.10)			
QT interval, Visit 4 (Month 9), n=246	3.9 (± 23.47)			
QT interval, Visit 5 (Month 12), n=232	5.0 (± 24.37)			
QT interval, Visit 8 (Month 24), n=157	3.4 (± 25.09)			
QT interval, Visit 11 (Month 36), n=112	8.8 (± 24.66)			
QT interval, Visit 14 (Month 48), n=96	7.0 (± 22.57)			
QT interval, Visit 17 (Month 60), n=89	7.9 (± 23.55)			
QT interval, Visit 20 (Month 72), n=56	12.4 (± 28.30)			
QT interval, Visit 23 (Month 84), n=32	8.4 (± 30.17)			
QT interval, Visit 26 (Month 96), n=23	4.0 (± 31.01)			
QT interval, Visit 29 (Month 108), n=13	0.8 (± 29.90)			
QT interval, Visit 32 (Month 120), n=1	64.0 (± 99999)			
QT interval, Follow up, n=254	1.2 (± 24.95)			
QTc Bazett interval, Visit 1 (Month 1, n=357	1.2 (± 18.07)			
QTc Bazett interval, Visit 2 (Month 3), n=324	1.6 (± 18.09)			
QTc Bazett interval, Visit 3 (Month 6), n=278	3.4 (± 16.97)			
QTc Bazett interval, Visit 4 (Month 9, n=246	4.4 (± 17.33)			
QTc Bazett interval, Visit 5 (Month 12), n=232	2.3 (± 16.61)			
QTc Bazett interval, Visit 8 (Month 24), n=157	6.6 (± 18.27)			
QTc Bazett interval, Visit 11 (Month 36), n=112	4.5 (± 18.10)			
QTc Bazett interval, Visit 14 (Month 48), n=96	5.6 (± 18.18)			
QTc Bazett interval, Visit 17 (Month 60), n=89	12.4 (± 25.68)			

QTc Bazett interval, Visit 20 (Month 72), n=56	15.6 (± 24.79)			
QTc Bazett interval, Visit 23 (Month 84), n=32	18.7 (± 23.90)			
QTc Bazett interval, Visit 26 (Month 96, n=23	19.7 (± 28.67)			
QTc Bazett interval, Visit 29 (Month 108), n=13	17.6 (± 21.09)			
QTc Bazett interval, Visit 32 (Month 120), n=1	0.7 (± 99999)			
QTc Bazett interval, Follow up, n=254	4.9 (± 18.39)			
QTc Friedericia interval, Visit 1 (Month 1),n=357	2.7 (± 15.72)			
QTc Friedericia interval Visit 2 (Month 3),n=324	2.7 (± 15.88)			
QTc Friedericia interval,Visit 3 (Month 6),n=278	4.0 (± 15.59)			
QTc Friedericia interval, Visit 4 (Month 9),n=246	4.1 (± 15.86)			
QTc Friedericia intervalVisit 5 (Month 12),n=232	3.2 (± 15.62)			
QTc Friedericia interval,Visit 8 (Month 24),n=157	5.4 (± 15.00)			
QTc Friedericia intervalVisit 11 (Month 36),n=112	5.9 (± 15.69)			
QTc Friedericia interval,Visit 14 (Month 48),n=96	6.1 (± 15.08)			
QTc Friedericia interval,Visit 17 (Month 60),n=89	10.8 (± 18.93)			
QTc Friedericia intervalVisit 20 (Month 72),n=56	14.4 (± 19.28)			
QTc Friedericia intervalVisit 23 (Month 84),n=32	15.0 (± 20.97)			
QTc Friedericia interval,Visit 26 (Month 96),n=23	14.3 (± 22.90)			
QTcFriedericia intervalVisit 29 (Month 108)n=13	11.6 (± 17.76)			
QTc Friedericia interval,Visit 32 (Month 120),n=1	23.7 (± 99999)			
QTcFriedericia interval, Follow up,n=254	3.5 (± 16.58)			

Notes:

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in alkaline phosphatase (Alk. Phos.), alanine amino transferase (ALT) and aspartate amino transferase (AST)

End point title	Change from Baseline in alkaline phosphatase (Alk. Phos.), alanine amino transferase (ALT) and aspartate amino transferase (AST) ^[17]
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End point description:

Clinical chemistry parameters included Alk. Phos., ALT and AST. The clinical laboratory evaluations were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
End point timeframe:	
Baseline and up to 122 months	
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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[18]			
Units: International units per liter				
arithmetic mean (standard deviation)				
Alk. Phos., Visit 1 (Month 1), n=352	-0.9 (± 14.47)			
Alk. Phos., Visit 1a (Month 2), n=1	-18.0 (± 99999)			
Alk. Phos., Visit 2 (Month 3), n=322	-1.5 (± 14.56)			
Alk. Phos., Visit 2a (Month 4), n=1	4.0 (± 99999)			
Alk. Phos., Visit 3 (Month 6), n=279	-1.2 (± 14.91)			
Alk. Phos., Visit 4 (Month 9), n=248	-3.0 (± 14.25)			
Alk. Phos., Visit 5 (Month 12), n=228	-1.9 (± 15.06)			
Alk. Phos., Visit 6 (Month 16), n=200	-1.8 (± 15.96)			
Alk. Phos., Visit 7 (Month 20), n=176	-3.6 (± 17.32)			
Alk. Phos., Visit 8 (Month 24), n=163	-4.0 (± 17.68)			
Alk. Phos., Visit 9 (Month 28), n=142	-3.1 (± 17.88)			
Alk. Phos., Visit 10 (Month 32), n=126	-4.6 (± 18.94)			
Alk. Phos., Visit 11 (Month 36), n=116	-6.2 (± 22.36)			
Alk. Phos., Visit 12 (Month 40), n=108	-4.8 (± 21.05)			
Alk. Phos., Visit 13 (Month 44), n=101	-5.8 (± 21.53)			
Alk. Phos., Visit 14 (Month 48), n=101	-7.2 (± 21.34)			
Alk. Phos., Visit 15 (Month 52), n=88	-2.5 (± 23.46)			
Alk. Phos., Visit 16 (Month 56), n=76	-0.1 (± 19.72)			
Alk. Phos., Visit 17 (Month 60), n=90	-5.1 (± 21.15)			
Alk. Phos., Visit 18 (Month 64), n=55	-2.0 (± 18.95)			
Alk. Phos., Visit 19 (Month 68), n=50	-0.6 (± 14.60)			
Alk. Phos., Visit 20 (Month 72), n=58	0.3 (± 23.56)			
Alk. Phos., Visit 21 (Month 76), n=40	0.8 (± 15.41)			
Alk. Phos., Visit 22 (Month 80), n=35	3.2 (± 19.97)			
Alk. Phos., Visit 23 (Month 84), n=32	0.2 (± 16.54)			
Alk. Phos., Visit 24 (Month 88), n=28	-0.1 (± 19.55)			
Alk. Phos., Visit 25 (Month 92), n=25	1.5 (± 21.27)			
Alk. Phos., Visit 26 (Month 96), n=26	4.8 (± 23.10)			
Alk. Phos., Visit 27 (Month 100), n=20	4.1 (± 14.67)			
Alk. Phos., Visit 28 (Month 104), n=16	8.6 (± 21.80)			
Alk. Phos., Visit 29 (Month 108), n=13	6.6 (± 17.94)			
Alk. Phos., Visit 30 (Month 112), n=4	1.8 (± 14.57)			
Alk. Phos., Visit 31 (Month 116), n=3	3.0 (± 3.61)			
Alk. Phos., Visit 32 (Month 120), n=1	1.0 (± 99999)			
Alk. Phos., Follow up, n=261	-0.4 (± 18.15)			
ALT, Visit 1 (Month 1), n=352	2.6 (± 20.05)			
ALT, Visit 1a (Month 2), n=1	-24.0 (± 99999)			

ALT, Visit 2 (Month 3), n=322	1.5 (± 16.57)			
ALT, Visit 2a (Month 4), n=1	45.0 (± 99999)			
ALT, Visit 3 (Month 6), n=278	1.3 (± 13.99)			
ALT, Visit 4 (Month 9), n=246	-0.2 (± 10.94)			
ALT, Visit 5 (Month 12), n=227	3.4 (± 28.91)			
ALT, Visit 6 (Month 16), n=200	1.3 (± 12.56)			
ALT, Visit 7 (Month 20), n=174	1.2 (± 17.23)			
ALT, Visit 8 (Month 24), n=163	0.5 (± 11.03)			
ALT, Visit 9 (Month 28), n=141	1.7 (± 16.40)			
ALT, Visit 10 (Month 32), n=126	1.0 (± 9.95)			
ALT, Visit 11 (Month 36), n=115	0.1 (± 8.11)			
ALT, Visit 12 (Month 40), n=107	0.9 (± 8.49)			
ALT, Visit 13 (Month 44), n=101	0.6 (± 8.39)			
ALT, Visit 14 (Month 48), n=99	0.5 (± 8.47)			
ALT, Visit 15 (Month 52), n=88	0.9 (± 9.83)			
ALT, Visit 16 (Month 56), n=75	1.3 (± 9.16)			
ALT, Visit 17 (Month 60), n=89	0.0 (± 8.06)			
ALT, Visit 18 (Month 64), n=54	-0.8 (± 7.12)			
ALT, Visit 19 (Month 68), n=50	-0.5 (± 7.57)			
ALT, Visit 20 (Month 72), n=58	0.6 (± 10.70)			
ALT, Visit 21 (Month 76), n=39	0.3 (± 10.65)			
ALT, Visit 22 (Month 80), n=35	0.1 (± 16.27)			
ALT, Visit 23 (Month 84), n=32	-2.3 (± 7.95)			
ALT, Visit 24 (Month 88), n=28	-4.1 (± 9.45)			
ALT, Visit 25 (Month 92), n=25	-4.2 (± 9.99)			
ALT, Visit 26 (Month 96), n=26	-1.6 (± 11.74)			
ALT, Visit 27 (Month 100), n=20	-3.2 (± 6.76)			
ALT, Visit 28 (Month 104), n=16	-3.1 (± 12.15)			
ALT, Visit 29 (Month 108), n=13	-3.6 (± 8.65)			
ALT, Visit 30 (Month 112), n=4	-5.3 (± 11.84)			
ALT, Visit 31 (Month 116), n=3	2.3 (± 18.15)			
ALT, Visit 32 (Month 120), n=1	1.0 (± 99999)			
ALT, Follow up, n=259	5.5 (± 64.04)			
AST, Visit 1 (Month 1), n=352	2.1 (± 13.00)			
AST, Visit 1a (Month 2), n=1	-65.0 (± 99999)			
AST, Visit 2 (Month 3), n=322	1.8 (± 14.76)			
AST, Visit 2a (Month 4), n=1	24.0 (± 99999)			
AST, Visit 3 (Month 6), n=278	1.0 (± 9.60)			
AST, Visit 4 (Month 9), n=246	0.7 (± 8.90)			
AST, Visit 5 (Month 12), n=227	3.0 (± 16.88)			
AST, Visit 6 (Month 16), n=200	1.7 (± 7.95)			
AST, Visit 7 (Month 20), n=174	2.7 (± 10.53)			
AST, Visit 8 (Month 24), n=162	2.7 (± 8.42)			
AST, Visit 9 (Month 28), n=141	3.3 (± 11.36)			
AST, Visit 10 (Month 32), n=126	3.3 (± 7.36)			
AST, Visit 11 (Month 36), n=115	3.2 (± 7.77)			
AST, Visit 12 (Month 40), n=106	3.6 (± 8.78)			
AST, Visit 13 (Month 44), n=101	3.7 (± 8.37)			
AST, Visit 14 (Month 48), n=99	3.9 (± 7.67)			
AST, Visit 15 (Month 52), n=87	2.7 (± 8.15)			
AST, Visit 16 (Month 56), n=74	3.7 (± 8.77)			

AST, Visit 17 (Month 60), n=89	3.6 (± 6.57)			
AST, Visit 18 (Month 64), n=54	2.1 (± 8.24)			
AST, Visit 19 (Month 68), n=50	2.3 (± 7.22)			
AST, Visit 20 (Month 72), n=58	4.0 (± 10.35)			
AST, Visit 21 (Month 76), n=39	3.9 (± 10.22)			
AST, Visit 22 (Month 80), n=35	3.8 (± 11.96)			
AST, Visit 23 (Month 84), n=32	1.9 (± 9.96)			
AST, Visit 24 (Month 88), n=28	3.5 (± 11.21)			
AST, Visit 25 (Month 92), n=25	1.3 (± 9.09)			
AST, Visit 26 (Month 96), n=26	2.5 (± 9.78)			
AST, Visit 27 (Month 100), n=20	1.6 (± 7.67)			
AST, Visit 28 (Month 104), n=16	3.2 (± 10.71)			
AST, Visit 29 (Month 108), n=13	0.7 (± 8.70)			
AST, Visit 30 (Month 112), n=4	-4.5 (± 10.60)			
AST, Visit 31 (Month 116), n=3	2.7 (± 23.03)			
AST, Visit 32 (Month 120), n=1	7.0 (± 99999)			
AST, Follow up, n=257	3.4 (± 36.36)			

Notes:

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in bicarbonate, calcium, chloride, cholesterol, non-fasting glucose, phosphorus, potassium, sodium and urea

End point title	Change from Baseline in bicarbonate, calcium, chloride, cholesterol, non-fasting glucose, phosphorus, potassium, sodium and urea ^[19]
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End point description:

Clinical chemistry parameters included bicarbonate, calcium, chloride, cholesterol, Non-fasting Glucose, phosphorus, potassium, sodium and urea. Approximately 7-milliliter sample of blood was drawn for clinical chemistry assays. The clinical laboratory evaluations were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[20]			
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Bicarbonate, Visit 1 (Month 1), n=344	-0.2 (± 3.02)			
Bicarbonate, Visit 1a (Month 2), n=1	-2.0 (± 99999)			

Bicarbonate, Visit 2 (Month 3), n=316	-0.3 (± 3.34)			
Bicarbonate, Visit 3 (Month 6), n=272	0.0 (± 3.06)			
Bicarbonate, Visit 4 (Month 9), n=243	-0.3 (± 3.22)			
Bicarbonate, Visit 5 (Month 12), n=221	-0.8 (± 3.18)			
Bicarbonate, Visit 6 (Month 16), n=196	-0.2 (± 3.11)			
Bicarbonate, Visit 7 (Month 20), n=171	-0.2 (± 3.22)			
Bicarbonate, Visit 8 (Month 24), n=159	-0.2 (± 3.26)			
Bicarbonate, Visit 9 (Month 28), n=140	-0.1 (± 3.44)			
Bicarbonate, Visit 10 (Month 32), n=126	-0.5 (± 3.74)			
Bicarbonate, Visit 11 (Month 36), n=116	-0.4 (± 3.54)			
Bicarbonate, Visit 12 (Month 40), n=107	0.0 (± 3.52)			
Bicarbonate, Visit 13 (Month 44), n=100	0.4 (± 3.41)			
Bicarbonate, Visit 14 (Month 48), n=101	-0.1 (± 3.56)			
Bicarbonate, Visit 15 (Month 52), n=86	0.5 (± 3.77)			
Bicarbonate, Visit 16 (Month 56), n=76	-0.1 (± 3.07)			
Bicarbonate, Visit 17 (Month 60), n=90	-0.1 (± 3.45)			
Bicarbonate, Visit 18 (Month 64), n=55	-0.7 (± 3.93)			
Bicarbonate, Visit 19 (Month 68), n=49	-1.1 (± 4.11)			
Bicarbonate, Visit 20 (Month 72), n=56	-1.2 (± 3.81)			
Bicarbonate, Visit 21 (Month 76), n=39	-0.2 (± 3.58)			
Bicarbonate, Visit 22 (Month 80), n=35	-1.0 (± 3.24)			
Bicarbonate, Visit 23 (Month 84), n=32	-1.3 (± 3.17)			
Bicarbonate, Visit 24 (Month 88), n=28	-0.7 (± 3.56)			
Bicarbonate, Visit 25 (Month 92), n=25	-1.8 (± 3.15)			
Bicarbonate, Visit 26 (Month 96), n=25	-1.0 (± 3.48)			
Bicarbonate, Visit 27 (Month 100), n=20	-1.3 (± 3.91)			
Bicarbonate, Visit 28 (Month 104), n=15	-1.9 (± 3.70)			
Bicarbonate, Visit 29 (Month 108), n=13	-1.8 (± 2.35)			
Bicarbonate, Visit 30 (Month 112), n=4	-2.0 (± 1.41)			
Bicarbonate, Visit 31 (Month 116), n=3	3.3 (± 6.11)			
Bicarbonate, Visit 32 (Month 120), n=1	2.0 (± 99999)			
Bicarbonate, Follow up, n=256	-1.0 (± 3.19)			
Calcium, Visit 1 (Month 1), n=352	0.000 (± 0.1187)			
Calcium, Visit 1a (Month 2), n=1	-0.250 (± 99999)			
Calcium, Visit 2 (Month 3), n=322	0.008 (± 0.1146)			
Calcium, Visit 2a (Month 4), n=1	-0.100 (± 99999)			
Calcium, Visit 3 (Month 6), n=279	0.018 (± 0.1169)			
Calcium, Visit 4 (Month 9), n=248	0.022 (± 0.1187)			
Calcium, Visit 5 (Month 12), n=228	0.010 (± 0.1269)			
Calcium, Visit 6 (Month 16), n=200	0.005 (± 0.1168)			
Calcium, Visit 7 (Month 20), n=176	0.005 (± 0.1118)			
Calcium, Visit 8 (Month 24), n=163	0.014 (± 0.1193)			
Calcium, Visit 9 (Month 28), n=142	0.015 (± 0.1154)			
Calcium, Visit 10 (Month 32), n=126	0.023 (± 0.1161)			

Calcium, Visit 11 (Month 36), n=116	0.017 (± 0.1274)			
Calcium, Visit 12 (Month 40), n=108	0.035 (± 0.1239)			
Calcium, Visit 13 (Month 44), n=101	0.028 (± 0.1168)			
Calcium, Visit 14 (Month 48), n=101	0.025 (± 0.1176)			
Calcium, Visit 15 (Month 52), n=88	0.020 (± 0.1225)			
Calcium, Visit 16 (Month 56), n=76	0.016 (± 0.1227)			
Calcium, Visit 17 (Month 60), n=90	0.008 (± 0.1172)			
Calcium, Visit 18 (Month 64), n=55	-0.007 (± 0.1270)			
Calcium, Visit 19 (Month 68), n=51	0.019 (± 0.1177)			
Calcium, Visit 20 (Month 72), n=58	-0.012 (± 0.1298)			
Calcium, Visit 21 (Month 76), n=40	0.020 (± 0.1257)			
Calcium, Visit 22 (Month 80), n=35	0.079 (± 0.1531)			
Calcium, Visit 23 (Month 84), n=32	0.038 (± 0.1113)			
Calcium, Visit 24 (Month 88), n=28	0.034 (± 0.1497)			
Calcium, Visit 25 (Month 92), n=25	0.089 (± 0.1560)			
Calcium, Visit 26 (Month 96), n=26	0.075 (± 0.1636)			
Calcium, Visit 27 (Month 100), n=20	0.121 (± 0.1552)			
Calcium, Visit 28 (Month 104), n=16	0.091 (± 0.1653)			
Calcium, Visit 29 (Month 108), n=13	0.080 (± 0.1297)			
Calcium, Visit 30 (Month 112), n=4	0.133 (± 0.1063)			
Calcium, Visit 31 (Month 116), n=3	0.053 (± 0.1124)			
Calcium, Visit 32 (Month 120), n=1	-0.040 (± 99999)			
Calcium, Follow up, n=261	0.031 (± 0.1245)			
Chloride, Visit 1 (Month 1), n=352	0.1 (± 3.48)			
Chloride, Visit 1a (Month 2), n=1	1.0 (± 99999)			
Chloride, Visit 2 (Month 3), n=322	0.3 (± 3.49)			
Chloride, Visit 2a (Month 4), n=1	2.0 (± 99999)			
Chloride, Visit 3 (Month 6), n=279	0.9 (± 3.52)			
Chloride, Visit 4 (Month 9), n=248	1.0 (± 3.46)			
Chloride, Visit 5 (Month 12), n=228	1.2 (± 3.75)			
Chloride, Visit 6 (Month 16), n=200	1.8 (± 3.73)			
Chloride, Visit 7 (Month 20), n=176	2.0 (± 4.09)			
Chloride, Visit 8 (Month 24), n=164	1.8 (± 4.42)			
Chloride, Visit 9 (Month 28), n=143	2.1 (± 4.45)			
Chloride, Visit 10 (Month 32), n=127	1.3 (± 4.22)			
Chloride, Visit 11 (Month 36), n=118	1.3 (± 4.55)			

Chloride, Visit 12 (Month 40), n=108	2.4 (± 4.68)			
Chloride, Visit 13 (Month 44), n=103	2.2 (± 4.59)			
Chloride, Visit 14 (Month 48), n=102	1.2 (± 4.91)			
Chloride, Visit 15 (Month 52), n=89	2.0 (± 4.63)			
Chloride, Visit 16 (Month 56), n=76	1.6 (± 4.51)			
Chloride, Visit 17 (Month 60), n=91	1.3 (± 5.16)			
Chloride, Visit 18 (Month 64), n=55	2.3 (± 3.33)			
Chloride, Visit 19 (Month 68), n=51	0.9 (± 4.22)			
Chloride, Visit 20 (Month 72), n=58	0.2 (± 5.33)			
Chloride, Visit 21 (Month 76), n=40	0.6 (± 4.11)			
Chloride, Visit 22 (Month 80), n=35	0.8 (± 3.30)			
Chloride, Visit 23 (Month 84), n=32	1.1 (± 4.33)			
Chloride, Visit 24 (Month 88), n=28	0.8 (± 3.94)			
Chloride, Visit 25 (Month 92), n=25	-0.4 (± 5.97)			
Chloride, Visit 26 (Month 96), n=26	-0.4 (± 4.56)			
Chloride, Visit 27 (Month 100), n=20	0.1 (± 5.31)			
Chloride, Visit 28 (Month 104), n=16	-1.1 (± 4.86)			
Chloride, Visit 29 (Month 108), n=13	-1.0 (± 5.66)			
Chloride, Visit 30 (Month 112), n=4	-3.0 (± 4.24)			
Chloride, Visit 31 (Month 116), n=3	-2.3 (± 5.03)			
Chloride, Visit 32 (Month 120), n=1	-3.0 (± 99999)			
Chloride, Follow up, n=261	0.3 (± 4.03)			
Cholesterol, Visit 1 (Month 1), n=352	0.066 (± 0.6255)			
Cholesterol, Visit 1a (Month 2), n=1	-0.360 (± 99999)			
Cholesterol, Visit 2 (Month 3), n=322	0.108 (± 0.6368)			
Cholesterol, Visit 2a (Month 4), n=1	-0.470 (± 99999)			
Cholesterol, Visit 3 (Month 6), n=279	0.062 (± 0.6978)			
Cholesterol, Visit 4 (Month 9), n=248	0.062 (± 0.7238)			
Cholesterol, Visit 5 (Month 12), n=228	0.075 (± 0.7074)			
Cholesterol, Visit 6 (Month 16), n=200	0.101 (± 0.7601)			
Cholesterol, Visit 7 (Month 20), n=176	0.001 (± 0.7820)			
Cholesterol, Visit 8 (Month 24), n=163	0.087 (± 0.8471)			
Cholesterol, Visit 9 (Month 28), n=142	-0.001 (± 0.7732)			
Cholesterol, Visit 10 (Month 32), n=126	-0.028 (± 0.8520)			
Cholesterol, Visit 11 (Month 36), n=116	-0.087 (± 0.7823)			
Cholesterol, Visit 12 (Month 40), n=108	-0.001 (± 0.7830)			
Cholesterol, Visit 13 (Month 44), n=101	-0.043 (± 0.8053)			
Cholesterol, Visit 14 (Month 48), n=101	-0.128 (± 0.7505)			
Cholesterol, Visit 15 (Month 52), n=88	-0.057 (± 0.7427)			
Cholesterol, Visit 16 (Month 56), n=76	0.026 (± 0.7354)			

Cholesterol, Visit 17 (Month 60), n=90	0.016 (± 0.8209)			
Cholesterol, Visit 18 (Month 64), n=55	0.054 (± 0.7474)			
Cholesterol, Visit 19 (Month 68), n=50	0.074 (± 0.8943)			
Cholesterol, Visit 20 (Month 72), n=58	-0.048 (± 0.8221)			
Cholesterol, Visit 21 (Month 76), n=40	0.103 (± 0.9056)			
Cholesterol, Visit 22 (Month 80), n=35	0.096 (± 0.8671)			
Cholesterol, Visit 23 (Month 84), n=32	0.077 (± 0.9637)			
Cholesterol, Visit 24 (Month 88), n=28	0.310 (± 0.8553)			
Cholesterol, Visit 25 (Month 92), n=25	0.327 (± 0.8143)			
Cholesterol, Visit 26 (Month 96), n=26	0.489 (± 1.0353)			
Cholesterol, Visit 27 (Month 100), n=20	0.370 (± 0.6675)			
Cholesterol, Visit 28 (Month 104), n=16	0.354 (± 0.6488)			
Cholesterol, Visit 29 (Month 108), n=13	0.141 (± 1.0346)			
Cholesterol, Visit 30 (Month 112), n=4	1.775 (± 0.9858)			
Cholesterol, Visit 31 (Month 116), n=3	1.123 (± 0.8723)			
Cholesterol, Visit 32 (Month 120), n=1	0.050 (± 99999)			
Cholesterol, Follow up, n=261	-0.070 (± 0.7047)			
Non-fasting Glucose, Visit 1 (Month 1), n=351	0.06 (± 0.885)			
Non-fasting Glucose, Visit 1a (Month 2), n=1	-0.30 (± 99999)			
Non-fasting Glucose, Visit 2 (Month 3), n=321	0.17 (± 1.002)			
Non-fasting Glucose, Visit 2a (Month 4), n=1	0.40 (± 99999)			
Non-fasting Glucose, Visit 3 (Month 6), n=278	0.12 (± 0.804)			
Non-fasting Glucose, Visit 4 (Month 9), n=247	0.16 (± 1.066)			
Non-fasting Glucose, Visit 5 (Month 12), n=227	0.16 (± 0.906)			
Non-fasting Glucose, Visit 6 (Month 16), n=199	0.10 (± 0.851)			
Non-fasting Glucose, Visit 7 (Month 20), n=176	0.02 (± 0.843)			
Non-fasting Glucose, Visit 8 (Month 24), n=161	0.12 (± 0.858)			
Non-fasting Glucose, Visit 9 (Month 28), n=142	0.04 (± 0.842)			
Non-fasting Glucose, Visit 10 (Month 32), n=126	0.03 (± 0.976)			
Non-fasting Glucose, Visit 11 (Month 36), n=115	0.08 (± 0.951)			
Non-fasting Glucose, Visit 12 (Month 40), n=108	0.06 (± 0.938)			

Non-fasting Glucose, Visit 13 (Month 44), n=100	0.07 (± 0.912)			
Non-fasting Glucose, Visit 14 (Month 48), n=101	-0.04 (± 0.881)			
Non-fasting Glucose, Visit 15 (Month 52), n=88	0.08 (± 0.745)			
Non-fasting Glucose, Visit 16 (Month 56), n=75	0.19 (± 0.931)			
Non-fasting Glucose, Visit 17 (Month 60), n=89	0.08 (± 0.773)			
Non-fasting Glucose, Visit 18 (Month 64), n=55	0.14 (± 1.125)			
Non-fasting Glucose, Visit 19 (Month 68), n=49	0.05 (± 0.816)			
Non-fasting Glucose, Visit 20 (Month 72), n=58	0.16 (± 0.878)			
Non-fasting Glucose, Visit 21 (Month 76), n=40	0.03 (± 0.895)			
Non-fasting Glucose, Visit 22 (Month 80), n=35	0.29 (± 1.116)			
Non-fasting Glucose, Visit 23 (Month 84), n=32	-0.01 (± 0.903)			
Non-fasting Glucose, Visit 24 (Month 88), n=28	0.14 (± 1.017)			
Non-fasting Glucose, Visit 25 (Month 92), n=25	0.28 (± 1.105)			
Non-fasting Glucose, Visit 26 (Month 96), n=26	0.50 (± 1.381)			
Non-fasting Glucose, Visit 27 (Month 100), n=20	0.18 (± 1.022)			
Non-fasting Glucose, Visit 28 (Month 104), n=16	0.74 (± 0.916)			
Non-fasting Glucose, Visit 29 (Month 108), n=13	0.25 (± 0.989)			
Non-fasting Glucose, Visit 30 (Month 112), n=4	0.65 (± 0.839)			
Non-fasting Glucose, Visit 31 (Month 116), n=3	0.70 (± 1.127)			
Non-fasting Glucose, Visit 32 (Month 120), n=1	-0.30 (± 99999)			
Non-fasting Glucose, Follow up, n=259	0.18 (± 1.068)			
Phosphorus, Visit 1 (Month 1), n=351	0.017 (± 0.1991)			
Phosphorus, Visit 1a (Month 2), n=1	0.030 (± 99999)			
Phosphorus, Visit 2 (Month 3), n=320	0.014 (± 0.2011)			
Phosphorus, Visit 2a (Month 4), n=1	0.160 (± 99999)			
Phosphorus, Visit 3 (Month 6), n=278	-0.001 (± 0.2125)			
Phosphorus, Visit 4 (Month 9), n=247	-0.009 (± 0.1912)			
Phosphorus, Visit 5 (Month 12), n=227	-0.016 (± 0.2130)			
Phosphorus, Visit 6 (Month 16), n=199	-0.023 (± 0.1994)			
Phosphorus, Visit 7 (Month 20), n=176	-0.022 (± 0.2224)			
Phosphorus, Visit 8 (Month 24), n=161	-0.012 (± 0.2332)			

Phosphorus, Visit 9 (Month 28), n=142	-0.011 (± 0.2146)			
Phosphorus, Visit 10 (Month 32), n=126	-0.005 (± 0.2231)			
Phosphorus, Visit 11 (Month 36), n=115	-0.026 (± 0.2284)			
Phosphorus, Visit 12 (Month 40), n=108	-0.030 (± 0.2585)			
Phosphorus, Visit 13 (Month 44), n=100	-0.026 (± 0.2241)			
Phosphorus, Visit 14 (Month 48), n=101	-0.050 (± 0.2331)			
Phosphorus, Visit 15 (Month 52), n=88	-0.054 (± 0.2207)			
Phosphorus, Visit 16 (Month 56), n=75	-0.052 (± 0.2465)			
Phosphorus, Visit 17 (Month 60), n=89	-0.047 (± 0.2419)			
Phosphorus, Visit 18 (Month 64), n=55	-0.059 (± 0.2540)			
Phosphorus, Visit 19 (Month 68), n=49	-0.047 (± 0.2905)			
Phosphorus, Visit 20 (Month 72), n=58	-0.076 (± 0.2502)			
Phosphorus, Visit 21 (Month 76), n=40	-0.074 (± 0.2503)			
Phosphorus, Visit 22 (Month 80), n=35	-0.071 (± 0.2930)			
Phosphorus, Visit 23 (Month 84), n=32	-0.068 (± 0.3006)			
Phosphorus, Visit 24 (Month 88), n=28	-0.115 (± 0.3460)			
Phosphorus, Visit 25 (Month 92), n=25	-0.130 (± 0.3251)			
Phosphorus, Visit 26 (Month 96), n=26	-0.098 (± 0.2820)			
Phosphorus, Visit 27 (Month 100), n=20	-0.197 (± 0.3030)			
Phosphorus, Visit 28 (Month 104), n=16	-0.261 (± 0.2665)			
Phosphorus, Visit 29 (Month 108), n=13	-0.300 (± 0.1534)			
Phosphorus, Visit 30 (Month 112), n=4	-0.065 (± 0.0603)			
Phosphorus, Visit 31 (Month 116), n=3	-0.260 (± 0.0000)			
Phosphorus, Visit 32 (Month 120), n=1	-0.320 (± 99999)			
Phosphorus, Follow up, n=260	-0.038 (± 0.2237)			
Potassium, Visit 1 (Month 1), n=351	-0.02 (± 0.426)			
Potassium, Visit 1a (Month 2), n=1	-0.40 (± 99999)			
Potassium, Visit 2 (Month 3), n=322	-0.05 (± 0.410)			
Potassium, Visit 2a (Month 4), n=1	0.40 (± 99999)			
Potassium, Visit 3 (Month 6), n=279	-0.04 (± 0.424)			
Potassium, Visit 4 (Month 9), n=247	-0.08 (± 0.427)			

Potassium, Visit 5 (Month 12), n=230	-0.07 (± 0.440)			
Potassium, Visit 6 (Month 16), n=199	0.00 (± 0.436)			
Potassium, Visit 7 (Month 20), n=174	-0.02 (± 0.434)			
Potassium, Visit 8 (Month 24), n=162	-0.03 (± 0.430)			
Potassium, Visit 9 (Month 28), n=143	-0.01 (± 0.434)			
Potassium, Visit 10 (Month 32), n=127	-0.01 (± 0.451)			
Potassium, Visit 11 (Month 36), n=116	-0.01 (± 0.457)			
Potassium, Visit 12 (Month 40), n=108	-0.05 (± 0.475)			
Potassium, Visit 13 (Month 44), n=102	-0.06 (± 0.466)			
Potassium, Visit 14 (Month 48), n=101	-0.01 (± 0.443)			
Potassium, Visit 15 (Month 52), n=89	-0.01 (± 0.436)			
Potassium, Visit 16 (Month 56), n=75	0.00 (± 0.506)			
Potassium, Visit 17 (Month 60), n=89	-0.05 (± 0.477)			
Potassium, Visit 18 (Month 64), n=55	-0.12 (± 0.468)			
Potassium, Visit 19 (Month 68), n=50	-0.03 (± 0.484)			
Potassium, Visit 20 (Month 72), n=58	-0.10 (± 0.485)			
Potassium, Visit 21 (Month 76), n=39	-0.11 (± 0.469)			
Potassium, Visit 22 (Month 80), n=35	-0.08 (± 0.461)			
Potassium, Visit 23 (Month 84), n=32	0.01 (± 0.523)			
Potassium, Visit 24 (Month 88), n=28	-0.05 (± 0.517)			
Potassium, Visit 25 (Month 92), n=25	-0.01 (± 0.488)			
Potassium, Visit 26 (Month 96), n=26	-0.02 (± 0.603)			
Potassium, Visit 27 (Month 100), n=20	-0.09 (± 0.609)			
Potassium, Visit 28 (Month 104), n=16	-0.18 (± 0.481)			
Potassium, Visit 29 (Month 108), n=13	-0.09 (± 0.647)			
Potassium, Visit 30 (Month 112), n=4	-0.38 (± 0.574)			
Potassium, Visit 31 (Month 116), n=3	-0.83 (± 0.611)			
Potassium, Visit 32 (Month 120), n=1	-0.30 (± 99999)			
Potassium, Follow up, n=258	-0.02 (± 0.456)			
Sodium, Visit 1 (Month 1), n=352	-0.3 (± 3.60)			
Sodium, Visit 1a (Month 2), n=1	0.0 (± 99999)			
Sodium, Visit 2 (Month 3), n=324	-0.1 (± 3.52)			
Sodium, Visit 2a (Month 4), n=1	1.0 (± 99999)			
Sodium, Visit 3 (Month 6), n=280	0.8 (± 3.49)			

Sodium, Visit 4 (Month 9), n=248	0.5 (± 3.50)			
Sodium, Visit 5 (Month 12), n=231	0.6 (± 3.84)			
Sodium, Visit 6 (Month 16), n=200	0.9 (± 3.81)			
Sodium, Visit 7 (Month 20), n=176	1.1 (± 3.88)			
Sodium, Visit 8 (Month 24), n=164	1.0 (± 4.38)			
Sodium, Visit 9 (Month 28), n=143	1.6 (± 4.36)			
Sodium, Visit 10 (Month 32), n=127	1.2 (± 4.08)			
Sodium, Visit 11 (Month 36), n=118	1.3 (± 5.15)			
Sodium, Visit 12 (Month 40), n=108	1.9 (± 4.25)			
Sodium, Visit 13 (Month 44), n=103	1.7 (± 4.06)			
Sodium, Visit 14 (Month 48), n=102	1.1 (± 4.44)			
Sodium, Visit 15 (Month 52), n=89	1.8 (± 4.29)			
Sodium, Visit 16 (Month 56), n=76	1.7 (± 3.75)			
Sodium, Visit 17 (Month 60), n=91	1.8 (± 4.62)			
Sodium, Visit 18 (Month 64), n=55	2.7 (± 3.32)			
Sodium, Visit 19 (Month 68), n=51	2.2 (± 3.63)			
Sodium, Visit 20 (Month 72), n=58	1.0 (± 4.46)			
Sodium, Visit 21 (Month 76), n=40	2.2 (± 3.82)			
Sodium, Visit 22 (Month 80), n=35	2.0 (± 3.11)			
Sodium, Visit 23 (Month 84), n=32	2.4 (± 3.72)			
Sodium, Visit 24 (Month 88), n=28	1.9 (± 3.85)			
Sodium, Visit 25 (Month 92), n=25	1.4 (± 5.45)			
Sodium, Visit 26 (Month 96), n=26	1.8 (± 4.48)			
Sodium, Visit 27 (Month 100), n=20	1.8 (± 4.76)			
Sodium, Visit 28 (Month 104), n=16	0.9 (± 3.14)			
Sodium, Visit 29 (Month 108), n=13	0.5 (± 4.58)			
Sodium, Visit 30 (Month 112), n=4	-0.3 (± 5.85)			
Sodium, Visit 31 (Month 116), n=3	0.7 (± 3.79)			
Sodium, Visit 32 (Month 120), n=1	-5.0 (± 99999)			
Sodium, Follow up, n=261	0.3 (± 3.91)			
Urea, Visit 1 (Month 1), n=351	0.583 (± 1.2933)			
Urea, Visit 1a (Month 2), n=1	2.860 (± 99999)			
Urea, Visit 2 (Month 3), n=322	0.606 (± 1.2846)			
Urea, Visit 2a (Month 4), n=1	1.780 (± 99999)			
Urea, Visit 3 (Month 6), n=279	0.623 (± 1.3294)			
Urea, Visit 4 (Month 9), n=248	0.642 (± 1.3781)			
Urea, Visit 5 (Month 12), n=228	0.599 (± 1.3323)			
Urea, Visit 6 (Month 16), n=200	0.656 (± 1.3598)			
Urea, Visit 7 (Month 20), n=176	0.750 (± 1.3893)			
Urea, Visit 8 (Month 24), n=163	0.652 (± 1.5332)			
Urea, Visit 9 (Month 28), n=142	0.578 (± 1.3512)			
Urea, Visit 10 (Month 32), n=126	0.748 (± 1.5680)			
Urea, Visit 11 (Month 36), n=117	0.552 (± 1.6650)			

Urea, Visit 12 (Month 40), n=108	0.794 (± 1.5456)			
Urea, Visit 13 (Month 44), n=102	0.697 (± 1.5664)			
Urea, Visit 14 (Month 48), n=101	0.792 (± 1.7321)			
Urea, Visit 15 (Month 52), n=88	0.828 (± 1.4226)			
Urea, Visit 16 (Month 56), n=76	0.742 (± 1.3964)			
Urea, Visit 17 (Month 60), n=90	0.778 (± 1.5392)			
Urea, Visit 18 (Month 64), n=55	0.766 (± 1.5980)			
Urea, Visit 19 (Month 68), n=51	0.791 (± 1.3485)			
Urea, Visit 20 (Month 72), n=58	0.794 (± 1.5895)			
Urea, Visit 21 (Month 76), n=40	1.152 (± 1.3824)			
Urea, Visit 22 (Month 80), n=35	0.939 (± 1.2432)			
Urea, Visit 23 (Month 84), n=32	0.781 (± 1.3376)			
Urea, Visit 24 (Month 88), n=28	0.791 (± 1.0485)			
Urea, Visit 25 (Month 92), n=25	0.529 (± 1.6380)			
Urea, Visit 26 (Month 96), n=26	0.811 (± 1.4025)			
Urea, Visit 27 (Month 100), n=20	0.501 (± 1.1668)			
Urea, Visit 28 (Month 104), n=16	0.536 (± 0.9589)			
Urea, Visit 29 (Month 108), n=13	0.523 (± 1.2418)			
Urea, Visit 30 (Month 112), n=4	0.983 (± 1.0297)			
Urea, Visit 31 (Month 116), n=3	0.837 (± 1.6082)			
Urea, Visit 32 (Month 120), n=1	-1.070 (± 99999)			
Urea, Follow up, n=260	0.158 (± 1.2473)			

Notes:

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in creatinine, total bilirubin and uric acid

End point title	Change from Baseline in creatinine, total bilirubin and uric
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End point description:

Clinical chemistry parameters included creatinine, total bilirubin and uric acid. The clinical laboratory evaluations were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could

not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[22]			
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Creatinine, Visit 1 (Month 1), n=351	1.8 (± 12.85)			
Creatinine, Visit 1a (Month 2), n=1	0.0 (± 99999)			
Creatinine, Visit 2 (Month 3), n=320	0.9 (± 8.49)			
Creatinine, Visit 2a (Month 4), n=1	9.0 (± 99999)			
Creatinine, Visit 3 (Month 6), n=278	0.7 (± 8.89)			
Creatinine, Visit 4 (Month 9), n=247	0.1 (± 9.04)			
Creatinine, Visit 5 (Month 12), n=227	0.0 (± 9.33)			
Creatinine, Visit 6 (Month 16), n=199	0.8 (± 10.14)			
Creatinine, Visit 7 (Month 20), n=176	0.6 (± 9.84)			
Creatinine, Visit 8 (Month 24), n=161	0.0 (± 8.81)			
Creatinine, Visit 9 (Month 28), n=142	-0.2 (± 9.98)			
Creatinine, Visit 10 (Month 32), n=126	1.3 (± 10.98)			
Creatinine, Visit 11 (Month 36), n=115	-0.3 (± 10.13)			
Creatinine, Visit 12 (Month 40), n=108	0.8 (± 10.30)			
Creatinine, Visit 13 (Month 44), n=101	0.5 (± 10.70)			
Creatinine, Visit 14 (Month 48), n=101	-0.3 (± 10.49)			
Creatinine, Visit 15 (Month 52), n=88	0.8 (± 9.55)			
Creatinine, Visit 16 (Month 56), n=75	1.1 (± 22.92)			
Creatinine, Visit 17 (Month 60), n=89	-1.6 (± 10.31)			
Creatinine, Visit 18 (Month 64), n=55	-0.7 (± 11.09)			
Creatinine, Visit 19 (Month 68), n=50	-0.9 (± 13.22)			
Creatinine, Visit 20 (Month 72), n=58	-3.6 (± 11.31)			
Creatinine, Visit 21 (Month 76), n=40	-0.7 (± 13.10)			
Creatinine, Visit 22 (Month 80), n=35	-2.2 (± 11.98)			
Creatinine, Visit 23 (Month 84), n=32	-1.4 (± 12.50)			
Creatinine, Visit 24 (Month 88), n=28	-4.1 (± 12.03)			
Creatinine, Visit 25 (Month 92), n=25	-3.2 (± 10.84)			
Creatinine, Visit 26 (Month 96), n=26	-2.6 (± 13.67)			
Creatinine, Visit 27 (Month 100), n=20	-3.9 (± 11.05)			
Creatinine, Visit 28 (Month 104), n=16	-4.2 (± 10.63)			
Creatinine, Visit 29 (Month 108), n=13	-7.7 (± 13.98)			
Creatinine, Visit 30 (Month 112), n=4	-6.3 (± 6.85)			
Creatinine, Visit 31 (Month 116), n=3	-18.7 (± 8.50)			
Creatinine, Visit 32 (Month 120), n=1	-19.0 (± 99999)			
Creatinine, Follow up, n=260	0.6 (± 9.99)			
Total Bilirubin, Visit 1 (Month 1), n=351	3.5 (± 3.41)			

Total Bilirubin, Visit 1a (Month 2), n=1	0.0 (± 99999)			
Total Bilirubin, Visit 2 (Month 3), n=322	3.5 (± 3.57)			
Total Bilirubin, Visit 2a (Month 4), n=1	6.0 (± 99999)			
Total Bilirubin, Visit 3 (Month 6), n=278	3.6 (± 3.62)			
Total Bilirubin, Visit 4 (Month 9), n=245	3.5 (± 3.63)			
Total Bilirubin, Visit 5 (Month 12), n=227	3.4 (± 3.56)			
Total Bilirubin, Visit 6 (Month 16), n=200	3.6 (± 3.69)			
Total Bilirubin, Visit 7 (Month 20), n=176	3.7 (± 3.60)			
Total Bilirubin, Visit 8 (Month 24), n=162	3.8 (± 3.70)			
Total Bilirubin, Visit 9 (Month 28), n=141	3.7 (± 3.57)			
Total Bilirubin, Visit 10 (Month 32), n=126	4.1 (± 3.68)			
Total Bilirubin, Visit 11 (Month 36), n=116	4.0 (± 3.82)			
Total Bilirubin, Visit 12 (Month 40), n=107	3.7 (± 3.44)			
Total Bilirubin, Visit 13 (Month 44), n=101	3.9 (± 3.46)			
Total Bilirubin, Visit 14 (Month 48), n=100	3.7 (± 3.67)			
Total Bilirubin, Visit 15 (Month 52), n=88	3.7 (± 3.37)			
Total Bilirubin, Visit 16 (Month 56), n=76	3.6 (± 3.47)			
Total Bilirubin, Visit 17 (Month 60), n=90	3.8 (± 3.36)			
Total Bilirubin, Visit 18 (Month 64), n=55	3.7 (± 3.68)			
Total Bilirubin, Visit 19 (Month 68), n=51	3.1 (± 4.12)			
Total Bilirubin, Visit 20 (Month 72), n=58	3.3 (± 3.69)			
Total Bilirubin, Visit 21 (Month 76), n=40	3.7 (± 4.02)			
Total Bilirubin, Visit 22 (Month 80), n=35	3.2 (± 4.22)			
Total Bilirubin, Visit 23 (Month 84), n=32	3.4 (± 4.01)			
Total Bilirubin, Visit 24 (Month 88), n=28	3.6 (± 5.04)			
Total Bilirubin, Visit 25 (Month 92), n=25	5.5 (± 4.57)			
Total Bilirubin, Visit 26 (Month 96), n=26	5.5 (± 6.59)			
Total Bilirubin, Visit 27 (Month 100), n=20	5.2 (± 6.29)			
Total Bilirubin, Visit 28 (Month 104), n=16	5.8 (± 5.01)			
Total Bilirubin, Visit 29 (Month 108), n=13	5.5 (± 8.32)			
Total Bilirubin, Visit 30 (Month 112), n=4	5.0 (± 3.65)			
Total Bilirubin, Visit 31 (Month 116), n=3	2.7 (± 6.03)			
Total Bilirubin, Visit 32 (Month 120), n=1	11.0 (± 99999)			

Total Bilirubin, Follow up, n=258	0.0 (± 2.92)			
Uric acid, Visit 1 (Month 1), n=352	2.1 (± 38.02)			
Uric acid, Visit 1a (Month 2), n=1	41.0 (± 99999)			
Uric acid, Visit 2 (Month 3), n=322	5.5 (± 42.30)			
Uric acid, Visit 2a (Month 4), n=1	107.0 (± 99999)			
Uric acid, Visit 3 (Month 6), n=279	4.3 (± 44.39)			
Uric acid, Visit 4 (Month 9), n=248	7.8 (± 41.60)			
Uric acid, Visit 5 (Month 12), n=228	5.3 (± 45.90)			
Uric acid, Visit 6 (Month 16), n=200	7.9 (± 49.61)			
Uric acid, Visit 7 (Month 20), n=176	8.8 (± 50.55)			
Uric acid, Visit 8 (Month 24), n=163	10.1 (± 54.77)			
Uric acid, Visit 9 (Month 28), n=142	7.7 (± 59.32)			
Uric acid, Visit 10 (Month 32), n=126	8.7 (± 55.37)			
Uric acid, Visit 11 (Month 36), n=116	9.8 (± 55.78)			
Uric acid, Visit 12 (Month 40), n=108	13.8 (± 64.68)			
Uric acid, Visit 13 (Month 44), n=101	13.4 (± 61.73)			
Uric acid, Visit 14 (Month 48), n=101	6.8 (± 61.69)			
Uric acid, Visit 15 (Month 52), n=88	14.2 (± 69.08)			
Uric acid, Visit 16 (Month 56), n=76	12.0 (± 60.26)			
Uric acid, Visit 17 (Month 60), n=90	14.7 (± 61.14)			
Uric acid, Visit 18 (Month 64), n=55	14.8 (± 58.21)			
Uric acid, Visit 19 (Month 68), n=50	25.2 (± 62.64)			
Uric acid, Visit 20 (Month 72), n=58	14.4 (± 62.38)			
Uric acid, Visit 21 (Month 76), n=40	25.5 (± 67.33)			
Uric acid, Visit 22 (Month 80), n=35	18.3 (± 63.64)			
Uric acid, Visit 23 (Month 84), n=32	21.4 (± 60.20)			
Uric acid, Visit 24 (Month 88), n=28	14.0 (± 72.96)			
Uric acid, Visit 25 (Month 92), n=25	29.6 (± 79.56)			
Uric acid, Visit 26 (Month 96), n=26	14.3 (± 69.23)			
Uric acid, Visit 27 (Month 100), n=20	14.2 (± 71.63)			
Uric acid, Visit 28 (Month 104), n=16	-1.8 (± 59.67)			
Uric acid, Visit 29 (Month 108), n=13	9.2 (± 74.02)			
Uric acid, Visit 30 (Month 112), n=4	46.3 (± 87.78)			
Uric acid, Visit 31 (Month 116), n=3	-8.0 (± 37.24)			
Uric acid, Visit 32 (Month 120), n=1	-23.0 (± 99999)			
Uric acid, Follow up, n=261	11.7 (± 45.09)			

Notes:

[22] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in total protein

End point title	Change from Baseline in total protein ^[23]
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End point description:

Clinical chemistry parameter included total protein. The clinical laboratory evaluation were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1

participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[24]			
Units: Grams per liter				
arithmetic mean (standard deviation)				
Total Protein, Visit 1 (Month 1), n=352	-1.1 (± 4.32)			
Total Protein, Visit 1a (Month 2), n=1	-12.0 (± 99999)			
Total Protein, Visit 2 (Month 3), n=322	-0.8 (± 4.34)			
Total Protein, Visit 2a (Month 4), n=1	-3.0 (± 99999)			
Total Protein, Visit 3 (Month 6), n=279	-1.1 (± 4.18)			
Total Protein, Visit 4 (Month 9), n=248	-1.8 (± 5.42)			
Total Protein, Visit 5 (Month 12), n=228	-1.6 (± 4.34)			
Total Protein, Visit 6 (Month 16), n=200	-1.3 (± 4.24)			
Total Protein, Visit 7 (Month 20), n=176	-1.8 (± 4.19)			
Total Protein, Visit 8 (Month 24), n=163	-1.5 (± 4.25)			
Total Protein, Visit 9 (Month 28), n=142	-1.5 (± 4.22)			
Total Protein, Visit 10 (Month 32), n=126	-1.3 (± 4.62)			
Total Protein, Visit 11 (Month 36), n=116	-2.1 (± 4.35)			
Total Protein, Visit 12 (Month 40), n=108	-1.9 (± 4.36)			
Total Protein, Visit 13 (Month 44), n=101	-1.8 (± 4.10)			
Total Protein, Visit 14 (Month 48), n=101	-2.0 (± 4.37)			
Total Protein, Visit 15 (Month 52), n=88	-1.9 (± 4.81)			
Total Protein, Visit 16 (Month 56), n=76	-2.1 (± 4.18)			
Total Protein, Visit 17 (Month 60), n=90	-2.4 (± 4.29)			
Total Protein, Visit 18 (Month 64), n=55	-2.2 (± 4.12)			
Total Protein, Visit 19 (Month 68), n=50	-2.2 (± 3.95)			
Total Protein, Visit 20 (Month 72), n=58	-3.0 (± 4.85)			
Total Protein, Visit 21 (Month 76), n=40	-1.8 (± 4.01)			
Total Protein, Visit 22 (Month 80), n=35	-0.6 (± 5.09)			
Total Protein, Visit 23 (Month 84), n=32	-2.2 (± 4.38)			
Total Protein, Visit 24 (Month 88), n=28	-1.9 (± 4.63)			
Total Protein, Visit 25 (Month 92), n=25	-1.2 (± 4.82)			
Total Protein, Visit 26 (Month 96), n=26	-1.1 (± 5.32)			
Total Protein, Visit 27 (Month 100), n=20	-0.9 (± 4.08)			
Total Protein, Visit 28 (Month 104), n=16	-0.2 (± 4.68)			
Total Protein, Visit 29 (Month 108), n=13	-2.1 (± 4.57)			

Total Protein, Visit 30 (Month 112), n=4	0.8 (± 2.36)			
Total Protein, Visit 31 (Month 116), n=3	-4.7 (± 0.58)			
Total Protein, Visit 32 (Month 120), n=1	-4.0 (± 99999)			
Total Protein, Follow up, n=261	-1.1 (± 4.75)			

Notes:

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelet count, white blood cells (WBC)

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelet count, white blood cells (WBC) ^[25]
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End point description:

Hematology parameters included eosinophils, basophils lymphocytes, monocytes, neutrophils, platelet count, and WBC. The clinical laboratory evaluations were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[26]			
Units: 10 ⁹ cells per Liter				
arithmetic mean (standard deviation)				
Basophils, Visit 1 (Month 1), n=345	0.003 (± 0.0261)			
Basophils, Visit 1a (Month 2), n=64	0.013 (± 0.0340)			
Basophils, Visit 2 (Month 3), n=309	0.001 (± 0.0251)			
Basophils, Visit 2a (Month 4), n=82	0.021 (± 0.0488)			
Basophils, Visit 3 (Month 6), n=273	0.003 (± 0.0340)			
Basophils, Visit 3a (Month 8), n=97	0.005 (± 0.0300)			
Basophils, Visit 4 (Month 9), n=239	0.000 (± 0.0222)			
Basophils, Visit 4a (Month 10), n=111	0.003 (± 0.0276)			
Basophils, Visit 5 (Month 12), n=225	0.002 (± 0.0188)			

Basophils, Visit 6 (Month 16), n=198	0.002 (± 0.0215)			
Basophils, Visit 7 (Month 20), n=173	0.003 (± 0.0230)			
Basophils, Visit 8 (Month 24), n=159	0.001 (± 0.0205)			
Basophils, Visit 9 (Month 28), n=139	0.005 (± 0.0200)			
Basophils, Visit 10 (Month 32), n=125	0.008 (± 0.0229)			
Basophils, Visit 11 (Month 36), n=112	0.005 (± 0.0200)			
Basophils, Visit 12 (Month 40), n=108	0.007 (± 0.0253)			
Basophils, Visit 13 (Month 44), n=98	0.002 (± 0.0157)			
Basophils, Visit 14 (Month 48), n=100	0.002 (± 0.0201)			
Basophils, Visit 15 (Month 52), n=88	0.005 (± 0.0249)			
Basophils, Visit 16 (Month 56), n=75	0.006 (± 0.0245)			
Basophils, Visit 17 (Month 60), n=89	0.006 (± 0.0186)			
Basophils, Visit 18 (Month 64), n=51	0.005 (± 0.0334)			
Basophils, Visit 19 (Month 68), n=50	0.006 (± 0.0184)			
Basophils, Visit 20 (Month 72), n=54	0.005 (± 0.0173)			
Basophils, Visit 21 (Month 76), n=39	0.009 (± 0.0226)			
Basophils, Visit 22 (Month 80), n=35	0.004 (± 0.0140)			
Basophils, Visit 23 (Month 84), n=32	0.009 (± 0.0178)			
Basophils, Visit 24 (Month 88), n=27	0.004 (± 0.0189)			
Basophils, Visit 25 (Month 92), n=25	0.013 (± 0.0281)			
Basophils, Visit 26 (Month 96), n=24	0.010 (± 0.0254)			
Basophils, Visit 27 (Month 100), n=20	0.010 (± 0.0192)			
Basophils, Visit 28 (Month 104), n=16	0.008 (± 0.0118)			
Basophils, Visit 29 (Month 108), n=13	0.005 (± 0.0156)			
Basophils, Visit 30 (Month 112), n=4	0.003 (± 0.0171)			
Basophils, Visit 31 (Month 116), n=3	-0.003 (± 0.0153)			
Basophils, Visit 32 (Month 120), n=1	-0.020 (± 99999)			
Basophils, Follow up, n=252	0.001 (± 0.0236)			
Eosinophils, Visit 1 (Month 1), n=345	-0.006 (± 0.1045)			
Eosinophils, Visit 1a (Month 2), n=64	-0.018 (± 0.0982)			
Eosinophils, Visit 2 (Month 3), n=309	-0.006 (± 0.1061)			

Eosinophils, Visit 2a (Month 4), n=82	-0.002 ($\pm$ 0.1274)			
Eosinophils, Visit 3 (Month 6), n=273	-0.009 ($\pm$ 0.0941)			
Eosinophils, Visit 3a (Month 8), n=97	-0.010 ($\pm$ 0.1142)			
Eosinophils, Visit 4 (Month 9), n=239	0.001 ($\pm$ 0.1148)			
Eosinophils, Visit 4a (Month 10), n=111	-0.003 ($\pm$ 0.1126)			
Eosinophils, Visit 5 (Month 12), n=225	-0.005 ($\pm$ 0.1160)			
Eosinophils, Visit 6 (Month 16), n=198	-0.012 ($\pm$ 0.1015)			
Eosinophils, Visit 7 (Month 20), n=173	-0.008 ($\pm$ 0.1070)			
Eosinophils, Visit 8 (Month 24), n=159	-0.007 ($\pm$ 0.0989)			
Eosinophils, Visit 9 (Month 28), n=139	-0.013 ($\pm$ 0.0972)			
Eosinophils, Visit 10 (Month 32), n=125	-0.007 ($\pm$ 0.0997)			
Eosinophils, Visit 11 (Month 36), n=112	-0.004 ($\pm$ 0.1042)			
Eosinophils, Visit 12 (Month 40), n=108	-0.006 ($\pm$ 0.1044)			
Eosinophils, Visit 13 (Month 44), n=98	-0.007 ($\pm$ 0.0962)			
Eosinophils, Visit 14 (Month 48), n=100	-0.018 ($\pm$ 0.0973)			
Eosinophils, Visit 15 (Month 52), n=88	-0.008 ($\pm$ 0.1115)			
Eosinophils, Visit 16 (Month 56), n=75	-0.008 ($\pm$ 0.1051)			
Eosinophils, Visit 17 (Month 60), n=88	0.009 ($\pm$ 0.1214)			
Eosinophils, Visit 18 (Month 64), n=51	-0.001 ($\pm$ 0.1298)			
Eosinophils, Visit 19 (Month 68), n=50	-0.008 ($\pm$ 0.1335)			
Eosinophils, Visit 20 (Month 72), n=54	-0.002 ($\pm$ 0.1235)			
Eosinophils, Visit 21 (Month 76), n=39	0.000 ($\pm$ 0.1365)			
Eosinophils, Visit 22 (Month 80), n=35	0.000 ($\pm$ 0.1352)			
Eosinophils, Visit 23 (Month 84), n=32	0.015 ($\pm$ 0.1251)			
Eosinophils, Visit 24 (Month 88), n=27	-0.022 ($\pm$ 0.1272)			
Eosinophils, Visit 25 (Month 92), n=25	-0.004 ($\pm$ 0.1064)			
Eosinophils, Visit 26 (Month 96), n=24	-0.007 ($\pm$ 0.1082)			
Eosinophils, Visit 27 (Month 100), n=20	0.032 ($\pm$ 0.1637)			
Eosinophils, Visit 28 (Month 104), n=16	0.041 ($\pm$ 0.1509)			
Eosinophils, Visit 29 (Month 108), n=13	0.062 ($\pm$ 0.1678)			
Eosinophils, Visit 30 (Month 112), n=4	0.185 ($\pm$ 0.1933)			

Eosinophils, Visit 31 (Month 116), n=3	0.043 (± 0.0603)			
Eosinophils, Visit 32 (Month 120), n=1	-0.020 (± 99999)			
Eosinophils, Follow up, n=252	-0.010 (± 0.1082)			
Lymphocytes, Visit 1 (Month 1), n=345	-0.127 (± 0.4854)			
Lymphocytes, Visit 1a (Month 2), n=64	-0.029 (± 0.5459)			
Lymphocytes, Visit 2 (Month 3), n=309	-0.147 (± 0.4446)			
Lymphocytes, Visit 2a (Month 4), n=82	-0.089 (± 0.5561)			
Lymphocytes, Visit 3 (Month 6), n=273	-0.124 (± 0.4476)			
Lymphocytes, Visit 3a (Month 8), n=97	-0.104 (± 0.4733)			
Lymphocytes, Visit 4 (Month 9), n=239	-0.137 (± 0.4833)			
Lymphocytes, Visit 4a (Month 10), n=111	0.007 (± 0.4505)			
Lymphocytes, Visit 5 (Month 12), n=225	-0.118 (± 0.4839)			
Lymphocytes, Visit 6 (Month 16), n=198	-0.130 (± 0.4605)			
Lymphocytes, Visit 7 (Month 20), n=173	-0.103 (± 0.4656)			
Lymphocytes, Visit 8 (Month 24), n=159	-0.091 (± 0.4387)			
Lymphocytes, Visit 9 (Month 28), n=139	-0.099 (± 0.4582)			
Lymphocytes, Visit 10 (Month 32), n=125	-0.103 (± 0.4502)			
Lymphocytes, Visit 11 (Month 36), n=112	-0.135 (± 0.4232)			
Lymphocytes, Visit 12 (Month 40), n=108	-0.114 (± 0.5521)			
Lymphocytes, Visit 13 (Month 44), n=98	-0.057 (± 0.4896)			
Lymphocytes, Visit 14 (Month 48), n=100	-0.117 (± 0.4672)			
Lymphocytes, Visit 15 (Month 52), n=88	-0.055 (± 0.4918)			
Lymphocytes, Visit 16 (Month 56), n=75	-0.049 (± 0.5077)			
Lymphocytes, Visit 17 (Month 60), n=88	-0.034 (± 0.5568)			
Lymphocytes, Visit 18 (Month 64), n=51	0.004 (± 0.5778)			
Lymphocytes, Visit 19 (Month 68), n=50	0.077 (± 0.5280)			
Lymphocytes, Visit 20 (Month 72), n=54	0.000 (± 0.5129)			
Lymphocytes, Visit 21 (Month 76), n=39	0.113 (± 0.5493)			
Lymphocytes, Visit 22 (Month 80), n=35	0.110 (± 0.5896)			
Lymphocytes, Visit 23 (Month 84), n=32	0.166 (± 0.4766)			
Lymphocytes, Visit 24 (Month 88), n=27	0.133 (± 0.5958)			

Lymphocytes, Visit 25 (Month 92), n=25	0.144 (± 0.3940)			
Lymphocytes, Visit 26 (Month 96), n=24	-0.001 (± 0.6195)			
Lymphocytes, Visit 27 (Month 100), n=20	0.172 (± 0.5272)			
Lymphocytes, Visit 28 (Month 104), n=16	0.141 (± 0.5226)			
Lymphocytes, Visit 29 (Month 108), n=13	0.193 (± 0.5144)			
Lymphocytes, Visit 30 (Month 112), n=4	0.278 (± 0.8945)			
Lymphocytes, Visit 31 (Month 116), n=3	0.367 (± 0.4038)			
Lymphocytes, Visit 32 (Month 120), n=1	-0.130 (± 99999)			
Lymphocytes, Follow up, n=252	0.022 (± 0.5031)			
Monocytes, Visit 1 (Month 1), n=345	0.024 (± 0.1425)			
Monocytes, Visit 1a (Month 2), n=64	0.085 (± 0.1846)			
Monocytes, Visit 2 (Month 3), n=309	0.017 (± 0.1580)			
Monocytes, Visit 2a (Month 4), n=82	0.071 (± 0.1850)			
Monocytes, Visit 3 (Month 6), n=273	0.022 (± 0.1610)			
Monocytes, Visit 3a (Month 8), n=97	0.073 (± 0.1581)			
Monocytes, Visit 4 (Month 9), n=239	0.022 (± 0.1518)			
Monocytes, Visit 4a (Month 10), n=111	0.080 (± 0.1653)			
Monocytes, Visit 5 (Month 12), n=225	0.028 (± 0.1563)			
Monocytes, Visit 6 (Month 16), n=198	0.023 (± 0.1598)			
Monocytes, Visit 7 (Month 20), n=173	0.019 (± 0.1661)			
Monocytes, Visit 8 (Month 24), n=159	0.038 (± 0.1840)			
Monocytes, Visit 9 (Month 28), n=139	0.056 (± 0.1646)			
Monocytes, Visit 10 (Month 32), n=125	0.047 (± 0.1597)			
Monocytes, Visit 11 (Month 36), n=112	0.049 (± 0.1649)			
Monocytes, Visit 12 (Month 40), n=108	0.040 (± 0.1750)			
Monocytes, Visit 13 (Month 44), n=98	0.037 (± 0.1780)			
Monocytes, Visit 14 (Month 48), n=100	0.033 (± 0.1442)			
Monocytes, Visit 15 (Month 52), n=88	0.065 (± 0.1720)			
Monocytes, Visit 16 (Month 56), n=75	0.043 (± 0.1632)			
Monocytes, Visit 17 (Month 60), n=88	0.044 (± 0.1736)			
Monocytes, Visit 18 (Month 64), n=51	0.028 (± 0.1644)			

Monocytes, Visit 19 (Month 68), n=50	0.027 (± 0.1253)			
Monocytes, Visit 20 (Month 72), n=54	0.039 (± 0.1201)			
Monocytes, Visit 21 (Month 76), n=39	0.078 (± 0.2002)			
Monocytes, Visit 22 (Month 80), n=35	0.046 (± 0.1629)			
Monocytes, Visit 23 (Month 84), n=32	0.064 (± 0.1596)			
Monocytes, Visit 24 (Month 88), n=27	0.065 (± 0.2083)			
Monocytes, Visit 25 (Month 92), n=25	0.057 (± 0.1956)			
Monocytes, Visit 26 (Month 96), n=24	0.035 (± 0.1405)			
Monocytes, Visit 27 (Month 100), n=20	0.119 (± 0.1604)			
Monocytes, Visit 28 (Month 104), n=16	0.039 (± 0.1903)			
Monocytes, Visit 29 (Month 108), n=13	0.068 (± 0.2342)			
Monocytes, Visit 30 (Month 112), n=4	0.030 (± 0.1985)			
Monocytes, Visit 31 (Month 116), n=3	-0.007 (± 0.0850)			
Monocytes, Visit 32 (Month 120), n=1	0.080 (± 99999)			
Monocytes, Follow up, n=252	0.022 (± 0.1754)			
Neutrophils, Visit 1 (Month 1), n=345	-0.143 (± 1.3093)			
Neutrophils, Visit 1a (Month 2), n=64	-0.142 (± 1.3123)			
Neutrophils, Visit 2 (Month 3), n=309	-0.045 (± 1.1768)			
Neutrophils, Visit 2a (Month 4), n=82	0.075 (± 1.4826)			
Neutrophils, Visit 3 (Month 6), n=273	-0.087 (± 1.3700)			
Neutrophils, Visit 3a (Month 8), n=97	-0.098 (± 1.3412)			
Neutrophils, Visit 4 (Month 9), n=239	0.032 (± 1.1933)			
Neutrophils, Visit 4a (Month 10), n=111	0.203 (± 1.3922)			
Neutrophils, Visit 5 (Month 12), n=225	0.015 (± 1.6014)			
Neutrophils, Visit 6 (Month 16), n=198	0.086 (± 1.3107)			
Neutrophils, Visit 7 (Month 20), n=173	0.121 (± 1.2780)			
Neutrophils, Visit 8 (Month 24), n=159	0.368 (± 1.4584)			
Neutrophils, Visit 9 (Month 28), n=139	0.188 (± 1.2575)			
Neutrophils, Visit 10 (Month 32), n=125	0.118 (± 1.1824)			
Neutrophils, Visit 11 (Month 36), n=112	0.057 (± 1.2868)			
Neutrophils, Visit 12 (Month 40), n=108	0.196 (± 1.1770)			

Neutrophils, Visit 13 (Month 44), n=98	0.243 ($\pm$ 1.4180)			
Neutrophils, Visit 14 (Month 48), n=100	0.095 ($\pm$ 1.2410)			
Neutrophils, Visit 15 (Month 52), n=88	0.432 ($\pm$ 1.4504)			
Neutrophils, Visit 16 (Month 56), n=75	0.412 ($\pm$ 1.4045)			
Neutrophils, Visit 17 (Month 60), n=88	0.416 ($\pm$ 1.3905)			
Neutrophils, Visit 18 (Month 64), n=51	0.296 ($\pm$ 1.2674)			
Neutrophils, Visit 19 (Month 68), n=50	0.436 ($\pm$ 1.0379)			
Neutrophils, Visit 20 (Month 72), n=54	0.552 ($\pm$ 1.3322)			
Neutrophils, Visit 21 (Month 76), n=39	0.639 ($\pm$ 1.5548)			
Neutrophils, Visit 22 (Month 80), n=35	0.346 ($\pm$ 1.3809)			
Neutrophils, Visit 23 (Month 84), n=32	0.560 ($\pm$ 1.4536)			
Neutrophils, Visit 24 (Month 88), n=27	0.366 ($\pm$ 1.8672)			
Neutrophils, Visit 25 (Month 92), n=25	0.130 ($\pm$ 1.9387)			
Neutrophils, Visit 26 (Month 96), n=24	0.707 ($\pm$ 1.7085)			
Neutrophils, Visit 27 (Month 100), n=20	0.247 ($\pm$ 1.6045)			
Neutrophils, Visit 28 (Month 104), n=16	0.458 ($\pm$ 1.1406)			
Neutrophils, Visit 29 (Month 108), n=13	-0.027 ($\pm$ 1.4607)			
Neutrophils, Visit 30 (Month 112), n=4	0.658 ($\pm$ 1.2219)			
Neutrophils, Visit 31 (Month 116), n=3	0.297 ($\pm$ 0.5320)			
Neutrophils, Visit 32 (Month 120), n=1	0.470 ($\pm$ 99999)			
Neutrophils, Follow up, n=252	-0.010 ($\pm$ 1.5258)			
Platelet Count, Visit 1 (Month 1), n=345	0.9 ($\pm$ 40.69)			
Platelet count, Visit 1a (Month 2), n=65	6.4 ($\pm$ 41.67)			
Platelet count, Visit 2 (Month 3), n=311	0.7 ($\pm$ 37.59)			
Platelet count, Visit 2a (Month 4), n=82	12.7 ($\pm$ 37.26)			
Platelet count, Visit 3 (Month 6), n=273	-1.7 ($\pm$ 41.28)			
Platelet count, Visit 3a (Month 8), n=99	-5.3 ($\pm$ 31.49)			
Platelet count, Visit 4 (Month 9), n=241	-7.1 ($\pm$ 37.88)			
Platelet count, Visit 4a (Month 10), n=108	-2.8 ($\pm$ 38.71)			
Platelet count, Visit 5 (Month 12), n=225	-8.6 ($\pm$ 35.57)			
Platelet count, Visit 6 (Month 16), n=196	-9.0 ($\pm$ 43.09)			
Platelet count, Visit 7 (Month 20), n=171	-15.8 ($\pm$ 41.13)			
Platelet count, Visit 8 (Month 24), n=162	-17.3 ($\pm$ 44.99)			
Platelet count, Visit 9 (Month 28), n=137	-18.0 ($\pm$ 44.47)			

Platelet count, Visit 10 (Month 32), n=124	-20.8 (± 38.96)			
Platelet count, Visit 11 (Month 36), n=114	-25.8 (± 42.66)			
Platelet count, Visit 12 (Month 40), n=108	-24.3 (± 39.96)			
Platelet count, Visit 13 (Month 44), n=98	-22.4 (± 37.92)			
Platelet count, Visit 14 (Month 48), n=98	-25.2 (± 37.88)			
Platelet count, Visit 15 (Month 52), n=84	-22.3 (± 40.93)			
Platelet count, Visit 16 (Month 56), n=75	-17.1 (± 50.19)			
Platelet count, Visit 17 (Month 60), n=88	-18.6 (± 46.11)			
Platelet count, Visit 18 (Month 64), n=54	-23.1 (± 38.78)			
Platelet count, Visit 19 (Month 68), n=50	-17.7 (± 42.66)			
Platelet count, Visit 20 (Month 72), n=53	-20.4 (± 51.90)			
Platelet count, Visit 21 (Month 76), n=40	-11.1 (± 55.97)			
Platelet count, Visit 22 (Month 80), n=34	-10.0 (± 57.22)			
Platelet count, Visit 23 (Month 84), n=31	-7.0 (± 50.20)			
Platelet count, Visit 24 (Month 88), n=25	-22.1 (± 29.77)			
Platelet count, Visit 25 (Month 92), n=25	-16.8 (± 40.54)			
Platelet count, Visit 26 (Month 96), n=24	-4.9 (± 43.76)			
Platelet count, Visit 27 (Month 100), n=20	1.9 (± 45.98)			
Platelet count, Visit 28 (Month 104), n=16	-6.3 (± 44.81)			
Platelet count, Visit 29 (Month 108), n=13	-9.5 (± 41.54)			
Platelet count, Visit 30 (Month 112), n=4	10.0 (± 32.44)			
Platelet count, Visit 31 (Month 116), n=3	-5.7 (± 30.09)			
Platelet count, Visit 32 (Month 120), n=1	25.0 (± 99999)			
Platelet count, Follow up, n=249	-9.4 (± 49.63)			
WBC, Visit 1 (Month 1), n=349	-0.25 (± 1.403)			
WBC, Visit 1a (Month 2), n=65	-0.11 (± 1.478)			
WBC, Visit 2 (Month 3), n=315	-0.22 (± 1.371)			
WBC, Visit 2a (Month 4), n=82	0.07 (± 1.648)			
WBC, Visit 3 (Month 6), n=278	-0.20 (± 1.531)			
WBC, Visit 3a (Month 8), n=99	-0.15 (± 1.537)			
WBC, Visit 4 (Month 9), n=244	-0.08 (± 1.356)			
WBC, Visit 4a (Month 10), n=113	0.28 (± 1.608)			

WBC, Visit 5 (Month 12), n=226	-0.09 (± 1.690)			
WBC, Visit 6 (Month 16), n=199	-0.06 (± 1.385)			
WBC, Visit 7 (Month 20), n=174	0.01 (± 1.468)			
WBC, Visit 8 (Month 24), n=164	0.25 (± 1.655)			
WBC, Visit 9 (Month 28), n=142	0.10 (± 1.367)			
WBC, Visit 10 (Month 32), n=126	0.09 (± 1.374)			
WBC, Visit 11 (Month 36), n=115	-0.05 (± 1.387)			
WBC, Visit 12 (Month 40), n=109	0.10 (± 1.514)			
WBC, Visit 13 (Month 44), n=98	0.21 (± 1.687)			
WBC, Visit 14 (Month 48), n=101	-0.01 (± 1.381)			
WBC, Visit 15 (Month 52), n=88	0.43 (± 1.648)			
WBC, Visit 16 (Month 56), n=76	0.37 (± 1.603)			
WBC, Visit 17 (Month 60), n=89	0.41 (± 1.663)			
WBC, Visit 18 (Month 64), n=54	0.33 (± 1.613)			
WBC, Visit 19 (Month 68), n=50	0.54 (± 1.376)			
WBC, Visit 20 (Month 72), n=55	0.57 (± 1.532)			
WBC, Visit 21 (Month 76), n=40	0.81 (± 1.940)			
WBC, Visit 22 (Month 80), n=35	0.52 (± 1.622)			
WBC, Visit 23 (Month 84), n=32	0.83 (± 1.599)			
WBC, Visit 24 (Month 88), n=27	0.57 (± 1.964)			
WBC, Visit 25 (Month 92), n=25	0.34 (± 2.114)			
WBC, Visit 26 (Month 96), n=24	0.75 (± 1.670)			
WBC, Visit 27 (Month 100), n=20	0.59 (± 1.809)			
WBC, Visit 28 (Month 104), n=16	0.70 (± 1.372)			
WBC, Visit 29 (Month 108), n=13	0.30 (± 1.614)			
WBC, Visit 30 (Month 112), n=4	1.18 (± 1.864)			
WBC, Visit 31 (Month 116), n=3	0.70 (± 0.800)			
WBC, Visit 32 (Month 120), n=1	0.40 (± 99999)			
WBC, Follow up, n=255	0.02 (± 1.738)			

Notes:

[26] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematocrit

End point title	Change from Baseline in hematocrit ^[27]
End point description:	
Blood samples for the assessment of clinical laboratory parameter hematocrit were collected at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).	
End point type	Primary
End point timeframe:	
Baseline and up to 122 months	

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[28]			
Units: Percentage of red blood cells in blood				
arithmetic mean (standard deviation)				
Hematocrit, Visit 1 (Month 1), n=340	-0.009 (± 0.0215)			
Hematocrit, Visit 1a (Month 2), n=63	-0.005 (± 0.0227)			
Hematocrit, Visit 2 (Month 3), n=308	-0.004 (± 0.0229)			
Hematocrit, Visit 2a (Month 4), n=79	-0.012 (± 0.0230)			
Hematocrit, Visit 3 (Month 6), n=274	-0.005 (± 0.0244)			
Hematocrit, Visit 3a (Month 8), n=95	-0.009 (± 0.0264)			
Hematocrit, Visit 4 (Month 9), n=231	-0.002 (± 0.0263)			
Hematocrit, Visit 4a (Month 10), n=111	-0.004 (± 0.0254)			
Hematocrit, Visit 5 (Month 12), n=223	-0.004 (± 0.0256)			
Hematocrit, Visit 6 (Month 16), n=196	-0.003 (± 0.0270)			
Hematocrit, Visit 7 (Month 20), n=166	-0.001 (± 0.0255)			
Hematocrit, Visit 8 (Month 24), n=160	0.000 (± 0.0275)			
Hematocrit, Visit 9 (Month 28), n=141	0.005 (± 0.0260)			
Hematocrit, Visit 10 (Month 32), n=122	0.004 (± 0.0285)			
Hematocrit, Visit 11 (Month 36), n=113	-0.001 (± 0.0301)			
Haematocrit, Visit 12 (Month 40), n=106	0.006 (± 0.0301)			
Hematocrit, Visit 13 (Month 44), n=95	0.003 (± 0.0274)			
Hematocrit, Visit 14 (Month 48), n=100	-0.003 (± 0.0286)			
Hematocrit, Visit 15 (Month 52), n=88	-0.001 (± 0.0289)			
Hematocrit, Visit 16 (Month 56), n=74	-0.001 (± 0.0230)			
Haematocrit, Visit 17 (Month 60), n=88	0.000 (± 0.0314)			
Hematocrit, Visit 18 (Month 64), n=51	0.009 (± 0.0270)			
Hematocrit, Visit 19 (Month 68), n=50	0.008 (± 0.0278)			
Hematocrit, Visit 20 (Month 72), n=55	0.004 (± 0.0287)			

Hematocrit, Visit 21 (Month 76), n=39	0.010 (± 0.0377)			
Hematocrit, Visit 22 (Month 80), n=34	0.015 (± 0.0303)			
Hematocrit, Visit 23 (Month 84), n=30	0.000 (± 0.0344)			
Hematocrit, Visit 24 (Month 88), n=26	0.005 (± 0.0294)			
Hematocrit, Visit 25 (Month 92), n=24	0.016 (± 0.0264)			
Hematocrit, Visit 26 (Month 96), n=24	0.013 (± 0.0258)			
Hematocrit, Visit 27 (Month 100), n=20	0.016 (± 0.0201)			
Hematocrit, Visit 28 (Month 104), n=16	0.016 (± 0.0203)			
Hematocrit, Visit 29 (Month 108), n=13	-0.002 (± 0.0268)			
Hematocrit, Visit 30 (Month 112), n=4	0.000 (± 0.0365)			
Hematocrit, Visit 31 (Month 116), n=3	0.033 (± 0.0666)			
Hematocrit, Visit 32 (Month 120), n=1	0.080 (± 99999)			
Hematocrit, Follow up, n=253	0.003 (± 0.0262)			

Notes:

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hemoglobin

End point title	Change from Baseline in hemoglobin ^[29]
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End point description:

The hematology parameters included hemoglobin. The clinical laboratory evaluations were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[30]			
Units: Grams per liter				
arithmetic mean (standard deviation)				
Hemoglobin, Visit 1 (Month 1), n=349	-2.6 (± 6.96)			

Hemoglobin, Visit 1a (Month 2), n=65	-1.8 (± 7.30)			
Hemoglobin, Visit 2 (Month 3), n=316	-0.8 (± 7.89)			
Hemoglobin, Visit 2a (Month 4), n=82	-3.3 (± 8.11)			
Hemoglobin, Visit 3 (Month 6), n=279	-1.3 (± 8.21)			
Hemoglobin, Visit 3a (Month 8), n=99	-3.0 (± 8.70)			
Hemoglobin, Visit 4 (Month 9), n=244	-0.7 (± 8.87)			
Hemoglobin, Visit 4a (Month 10), n=113	-2.0 (± 8.41)			
Hemoglobin, Visit 5 (Month 12), n=226	-1.4 (± 8.64)			
Hemoglobin, Visit 6 (Month 16), n=199	-0.4 (± 8.83)			
Hemoglobin, Visit 7 (Month 20), n=174	-0.6 (± 9.01)			
Hemoglobin, Visit 8 (Month 24), n=164	-0.3 (± 8.58)			
Hemoglobin, Visit 9 (Month 28), n=142	1.2 (± 8.99)			
Hemoglobin, Visit 10 (Month 32), n=126	0.3 (± 9.58)			
Hemoglobin, Visit 11 (Month 36), n=115	-1.0 (± 10.12)			
Hemoglobin, Visit 12 (Month 40), n=109	0.4 (± 9.78)			
Hemoglobin, Visit 13 (Month 44), n=98	-0.1 (± 9.44)			
Hemoglobin, Visit 14 (Month 48), n=101	-1.6 (± 9.57)			
Hemoglobin, Visit 15 (Month 52), n=88	-1.6 (± 9.75)			
Hemoglobin, Visit 16 (Month 56), n=76	-2.3 (± 7.47)			
Hemoglobin, Visit 17 (Month 60), n=89	-2.4 (± 10.14)			
Hemoglobin, Visit 18 (Month 64), n=54	-1.1 (± 8.76)			
Hemoglobin, Visit 19 (Month 68), n=50	-0.4 (± 9.42)			
Hemoglobin, Visit 20 (Month 72), n=55	-2.5 (± 10.78)			
Hemoglobin, Visit 21 (Month 76), n=40	-1.5 (± 11.67)			
Hemoglobin, Visit 22 (Month 80), n=35	-0.8 (± 9.66)			
Hemoglobin, Visit 23 (Month 84), n=32	-3.6 (± 11.61)			
Hemoglobin, Visit 24 (Month 88), n=27	-3.0 (± 9.46)			
Hemoglobin, Visit 25 (Month 92), n=25	-2.3 (± 8.09)			
Hemoglobin, Visit 26 (Month 96), n=24	-4.0 (± 8.26)			
Hemoglobin, Visit 27 (Month 100), n=20	-2.8 (± 5.82)			
Hemoglobin, Visit 28 (Month 104), n=16	-2.9 (± 9.54)			
Hemoglobin, Visit 29 (Month 108), n=13	-8.1 (± 8.56)			
Hemoglobin, Visit 30 (Month 112), n=4	-12.5 (± 6.14)			
Hemoglobin, Visit 31 (Month 116), n=3	3.0 (± 22.52)			
Hemoglobin, Visit 32 (Month 120), n=1	25.0 (± 99999)			
Hemoglobin, Follow up, n=256	-0.1 (± 8.89)			

Notes:

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematology parameter red blood cells (RBC)

End point title	Change from Baseline in hematology parameter red blood cells (RBC) ^[31]
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End point description:

The hematology parameters included RBC. The clinical laboratory evaluation were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed

(represented by n=X in the category titles).

End point type	Primary
End point timeframe:	
Baseline and up to 122 months	

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[32]			
Units: 10 ¹² cells per liter				
arithmetic mean (standard deviation)				
RBC, Visit 1 (Month 1), n=349	-0.07 (± 0.226)			
RBC, Visit 1a (Month 2), n=65	0.00 (± 0.236)			
RBC, Visit 2 (Month 3), n=316	-0.02 (± 0.237)			
RBC, Visit 2a (Month 4), n=82	-0.06 (± 0.233)			
RBC, Visit 3 (Month 6), n=279	-0.04 (± 0.243)			
RBC, Visit 3a (Month 8), n=99	-0.05 (± 0.269)			
RBC, Visit 4 (Month 9), n=244	-0.03 (± 0.256)			
RBC, Visit 4a (Month 10), n=113	-0.02 (± 0.235)			
RBC, Visit 5 (Month 12), n=226	-0.04 (± 0.255)			
RBC, Visit 6 (Month 16), n=199	-0.01 (± 0.264)			
RBC, Visit 7 (Month 20), n=174	-0.02 (± 0.243)			
RBC, Visit 8 (Month 24), n=164	-0.03 (± 0.281)			
RBC, Visit 9 (Month 28), n=142	0.00 (± 0.271)			
RBC, Visit 10 (Month 32), n=126	-0.05 (± 0.286)			
RBC, Visit 11 (Month 36), n=115	-0.09 (± 0.283)			
RBC, Visit 12 (Month 40), n=109	-0.02 (± 0.275)			
RBC, Visit 13 (Month 44), n=98	-0.06 (± 0.287)			
RBC, Visit 14 (Month 48), n=101	-0.10 (± 0.280)			
RBC, Visit 15 (Month 52), n=88	-0.08 (± 0.285)			
RBC, Visit 16 (Month 56), n=76	-0.08 (± 0.252)			
RBC, Visit 17 (Month 60), n=89	-0.07 (± 0.323)			
RBC, Visit 18 (Month 64), n=54	-0.01 (± 0.263)			
RBC, Visit 19 (Month 68), n=50	0.01 (± 0.255)			
RBC, Visit 20 (Month 72), n=55	-0.03 (± 0.239)			

RBC, Visit 21 (Month 76), n=40	0.02 (± 0.346)			
RBC, Visit 22 (Month 80), n=35	0.09 (± 0.338)			
RBC, Visit 23 (Month 84), n=32	0.00 (± 0.290)			
RBC, Visit 24 (Month 88), n=27	0.00 (± 0.314)			
RBC, Visit 25 (Month 92), n=25	0.05 (± 0.337)			
RBC, Visit 26 (Month 96), n=24	0.06 (± 0.317)			
RBC, Visit 27 (Month 100), n=20	0.13 (± 0.251)			
RBC, Visit 28 (Month 104), n=16	0.14 (± 0.365)			
RBC, Visit 29 (Month 108), n=13	-0.04 (± 0.328)			
RBC, Visit 30 (Month 112), n=4	0.08 (± 0.386)			
RBC, Visit 31 (Month 116), n=3	0.10 (± 0.346)			
RBC, Visit 32 (Month 120), n=1	0.00 (± 99999)			
RBC, Follow up, n=256	-0.01 (± 0.263)			

Notes:

[32] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine specific gravity

End point title	Change from Baseline in urine specific gravity ^[33]
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End point description:

Urine specific gravity is a measure of the concentration of solutes in the urine. It measures the ratio of urine density compared with water density and provides information on the kidney's ability to concentrate urine. Urinalysis assessments were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[34]			
Units: Ratio				
arithmetic mean (standard deviation)				
Specific gravity, Visit 1 (Month 1), n=348	-0.0011 (± 0.00936)			
Specific gravity, Visit 1a (Month 2), n=1	0.0000 (± 99999)			
Specific gravity, Visit 2 (Month 3), n=312	-0.0011 (± 0.00918)			
Specific gravity, Visit 3 (Month 6), n=270	0.0003 (± 0.00896)			

Specific gravity, Visit 4 (Month 9), n=243	0.0002 (± 0.00984)			
Specific gravity, Visit 5 (Month 12), n=221	-0.0010 (± 0.01014)			
Specific gravity, Visit 6 (Month 16), n=196	0.0006 (± 0.01016)			
Specific gravity, Visit 7 (Month 20), n=170	0.0015 (± 0.00901)			
Specific gravity, Visit 8 (Month 24), n=157	0.0002 (± 0.01015)			
Specific gravity, Visit 9 (Month 28), n=137	0.0007 (± 0.00922)			
Specific gravity, Visit 10 (Month 32), n=124	0.0001 (± 0.00986)			
Specific gravity, Visit 11 (Month 36), n=111	-0.0016 (± 0.01058)			
Specific gravity, Visit 12 (Month 40), n=106	0.0004 (± 0.01007)			
Specific gravity, Visit 13 (Month 44), n=97	0.0004 (± 0.00944)			
Specific gravity, Visit 14 (Month 48), n=99	0.0000 (± 0.01019)			
Specific gravity, Visit 15 (Month 52), n=83	-0.0100 (± 0.10022)			
Specific gravity, Visit 16 (Month 56), n=71	0.0003 (± 0.01089)			
Specific gravity, Visit 17 (Month 60), n=84	-0.0008 (± 0.01022)			
Specific gravity, Visit 18 (Month 64), n=53	0.0006 (± 0.00894)			
Specific gravity, Visit 19 (Month 68), n=50	0.0014 (± 0.01052)			
Specific gravity, Visit 20 (Month 72), n=55	-0.0021 (± 0.00882)			
Specific gravity, Visit 21 (Month 76), n=39	0.0030 (± 0.00837)			
Specific gravity, Visit 22 (Month 80), n=35	0.0015 (± 0.00939)			
Specific gravity, Visit 23 (Month 84), n=31	0.0024 (± 0.00917)			
Specific gravity, Visit 24 (Month 88), n=28	0.0043 (± 0.00994)			
Specific gravity, Visit 25 (Month 92), n=25	0.0046 (± 0.00861)			
Specific gravity, Visit 26 (Month 96), n=26	0.0035 (± 0.00857)			
Specific gravity, Visit 27 (Month 100), n=20	0.0029 (± 0.00718)			
Specific gravity, Visit 28 (Month 104), n=16	0.0026 (± 0.00713)			
Specific gravity, Visit 29 (Month 108), n=13	0.0020 (± 0.00709)			
Specific gravity, Visit 30 (Month 112), n=4	0.0020 (± 0.00673)			
Specific gravity, Visit 31 (Month 116), n=3	0.0030 (± 0.01082)			
Specific gravity, Visit 32 (Month 120), n=1	-0.0010 (± 99999)			
Specific gravity, Follow up, n=247	0.0008 (± 0.00889)			

Notes:

[34] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine potential of hydrogen (pH)

End point title	Change from Baseline in urine potential of hydrogen (pH) ^[35]
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End point description:

Urinalysis parameters included urine pH. pH is calculated on a scale of 0 to 14, such that, the lower the number, more acidic the urine and higher the number, more alkaline the urine with 7 being neutral. Urinalysis assessments were performed at all study visits during the Open-Label Treatment Phase. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[36]			
Units: Unit on a pH scale				
arithmetic mean (standard deviation)				
pH, Visit 1 (Month 1), n=349	-0.13 (± 0.685)			
pH, Visit 1a (Month 2), n=1	0.50 (± 99999)			
pH, Visit 2 (Month 3), n=313	-0.09 (± 0.699)			
pH, Visit 3 (Month 6), n=270	-0.07 (± 0.634)			
pH, Visit 4 (Month 9), n=245	0.02 (± 0.633)			
pH, Visit 5 (Month 12), n=222	-0.02 (± 0.616)			
pH, Visit 6 (Month 16), n=196	0.07 (± 0.651)			
pH, Visit 7 (Month 20), n=170	0.04 (± 0.686)			
pH, Visit 8 (Month 24), n=158	0.09 (± 0.672)			
pH, Visit 9 (Month 28), n=138	0.17 (± 0.787)			
pH, Visit 10 (Month 32), n=124	0.17 (± 0.715)			
pH, Visit 11 (Month 36), n=111	0.26 (± 0.663)			
pH, Visit 12 (Month 40), n=107	0.30 (± 0.700)			
pH, Visit 13 (Month 44), n=97	0.36 (± 0.736)			
pH, Visit 14 (Month 48), n=99	0.38 (± 0.722)			
pH, Visit 15 (Month 52), n=83	0.27 (± 0.621)			

pH, Visit 16 (Month 56), n=71	0.34 (± 0.840)			
pH, Visit 17 (Month 60), n=84	0.32 (± 0.662)			
pH, Visit 18 (Month 64), n=53	0.33 (± 0.627)			
pH, Visit 19 (Month 68), n=50	0.42 (± 0.785)			
pH, Visit 20 (Month 72), n=55	0.27 (± 0.686)			
pH, Visit 21 (Month 76), n=39	0.36 (± 0.688)			
pH, Visit 22 (Month 80), n=35	0.23 (± 0.657)			
pH, Visit 23 (Month 84), n=31	0.35 (± 0.661)			
pH, Visit 24 (Month 88), n=28	0.29 (± 0.517)			
pH, Visit 25 (Month 92), n=25	0.36 (± 0.621)			
pH, Visit 26 (Month 96), n=26	0.21 (± 0.551)			
pH, Visit 27 (Month 100), n=20	0.45 (± 0.724)			
pH, Visit 28 (Month 104), n=16	0.13 (± 0.342)			
pH, Visit 29 (Month 108), n=13	0.77 (± 0.753)			
pH, Visit 30 (Month 112), n=4	0.50 (± 0.577)			
pH, Visit 31 (Month 116), n=3	-0.17 (± 0.764)			
pH, Visit 32 (Month 120), n=1	0.00 (± 99999)			
pH, Follow up, n=248	0.22 (± 0.746)			

Notes:

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Post-Void Residual (PVR) bladder ultrasound volume ^[37]
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End point description:

The post-void residual urine volume in the bladder was evaluated by transabdominal ultrasound. The urine bladder was sonicated from two directions perpendicular to one another, and the volume calculated automatically. A PVR bladder ultrasound to assess urinary retention was performed during the first year at Months 1, 3 and 12 and at the end of each 12 month study cycle that the participant was enrolled (i.e., second year, third year, fourth year, etc.) in the Open-Label Treatment Phase of the study. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category title).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[38]			
Units: Milliliters				
arithmetic mean (standard deviation)				
PVR urine volume, Visit 1 (Month 1), n=337	4.6 (± 52.10)			
PVR urine volume, Visit 2 (Month 3), n=307	4.1 (± 40.88)			
PVR urine volume, Visit 5 (Month 12), n=223	4.1 (± 52.38)			
PVR urine volume, Visit 8 (Month 24), n=111	5.5 (± 67.28)			
PVR urine volume, Visit 11 (Month 36), n=106	5.0 (± 46.29)			
PVR urine volume, Visit 14 (Month 48), n=96	-2.3 (± 39.69)			
PVR urine volume, Visit 17 (Month 60), n=77	22.2 (± 87.43)			
PVR urine volume, Visit 20 (Month 72), n=53	7.1 (± 49.87)			
PVR urine volume, Visit 23 (Month 84), n=29	15.7 (± 74.06)			
PVR urine volume, Visit 26 (Month 96), n=24	2.0 (± 38.54)			
PVR urine volume, Visit 29 (Month 108), n=10	21.9 (± 63.58)			
PVR urine volume, Follow up, n=186	-4.0 (± 47.11)			

Notes:

[38] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in the urinary voiding function [UVF] (assessed using the American Urological Association [AUA] Symptom Index)

End point title	Change from Baseline in the urinary voiding function [UVF] (assessed using the American Urological Association [AUA] Symptom Index) ^[39]
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End point description:

AUA Symptom Index was completed during the first year at Months 1, 3, 12 and at the end of each 12 month study cycle that the participant was enrolled in the Open-Label Treatment Phase (second, third, fourth year) to assess the participant UVF. The questions were scored on a scale of 0 to 5, with 0 (not at all) to 5 (almost always). A Symptom Index is determined by adding the scores. The lowest possible score is 0 and the highest possible score is 35, which would represent the highest level of pain and discomfort. Baseline assessment in this OLE study was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed represented by (n=x).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[40]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
AUA Overall Score, Visit 1 (Month 1), n=348	-0.4 (± 3.82)			
AUA Overall Score, Visit 2 (Month 3), n=325	-0.5 (± 3.80)			
AUA Overall Score, Visit 5 (Month 12), n=228	-0.5 (± 3.58)			
AUA Overall Score, Visit 8 (Month 24), n=114	-0.5 (± 3.84)			
AUA Overall Score, Visit 11 (Month 36), n=115	-0.3 (± 5.22)			
AUA Overall Score, Visit 14 (Month 48), n=102	-0.6 (± 4.89)			
AUA Overall Score, Visit 17 (Month 60), n=87	-0.4 (± 5.02)			
AUA Overall Score, Visit 20 (Month 72), n=56	-0.1 (± 5.52)			
AUA Overall Score, Visit 23 (Month 84), n=32	0.8 (± 6.61)			
AUA Overall Score, Visit 26 (Month 96), n=26	0.5 (± 5.58)			
AUA Overall Score, Visit 29 (Month 108), n=13	0.0 (± 1.68)			
AUA Overall Score, Visit 32 (Month 120), n=1	0.0 (± 99999)			
AUA Overall Score, Follow up, n=217	0.0 (± 4.43)			

Notes:

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Quality of Life in Epilepsy-31-Problems (QOLIE-31-P) Questionnaire

End point title	Change from Baseline in Quality of Life in Epilepsy-31-Problems (QOLIE-31-P) Questionnaire ^[41]
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End point description:

The QOLIE-31-P questionnaire contained 30 items. The subscale scores (seizure worry, overall QOL, emotional well-being, energy-fatigue, cognitive, medication effects, social functioning), the final QOLIE-31-P score and the weighted total score (overall assessment) were calculated according to the scoring algorithm defined by the author. Scores range from 0 to 100 with higher scores indicating better function. Baseline was defined as the last assessment of that endpoint in VRX-RET-E22-302 taken prior to the first active treatment with retigabine. Change from Baseline was calculated by subtracting the Baseline value from the post Baseline values. 99999 indicates standard deviation could not be calculated as only 1 participant was analyzed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[42]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Final QOLIE-31-P Score, Visit 2 (Month 3), n=296	1.33 (± 14.409)			
Final QOLIE-31-P Score, Visit 3 (Month 6), n=262	0.87 (± 14.618)			
Final QOLIE-31-P Score, Visit 4 (Month 9), n=229	0.27 (± 14.365)			
Final QOLIE-31-P Score, Visit 5 (Month 12), n=214	1.24 (± 14.498)			
Final QOLIE-31-P Score, Visit 8 (Month 24), n=142	3.76 (± 12.406)			
Final QOLIE-31-P Score, Visit 11 (Month 36), n=97	2.77 (± 13.784)			
Final QOLIE-31-P Score, Visit 14 (Month 48), n=83	0.78 (± 13.976)			
Final QOLIE-31-P Score Visit 17 (Month 60), n=68	2.37 (± 15.197)			
Final QOLIE-31-P Score Visit 20 (Month 72), n=47	3.07 (± 16.172)			
Final QOLIE-31-P Score Visit 23 (Month 84), n=26	4.31 (± 13.849)			
Final QOLIE-31-P Score Visit 26 (Month 96), n=24	4.07 (± 11.745)			
Final QOLIE-31-P Score Visit 29 (Month 108), n=12	6.35 (± 14.783)			
Final QOLIE-31-P Score Visit 32 (Month 120), n=1	14.36 (± 99999)			
Final QOLIE-31-P Score, Follow up, n=224	-0.83 (± 14.256)			

Notes:

[42] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with Abnormal Results of Physical Examination

End point title	Percentage of participants with Abnormal Results of Physical Examination ^[43]
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End point description:

A complete physical examination was performed at the end of each 12 month study cycle (i.e., first year, second year, third year, etc.) during the Open-Label Treatment Phase. The investigator assessed the skin at every clinic visit. If abnormal skin discoloration was confirmed, the participant continued to be followed by the dermatologist. If the abnormal skin discoloration was not confirmed, the investigator resumed assessing the participants skin at all scheduled clinic visits. Only data for abnormal values on physical examination have been presented. Only those participants available at the specified time points were analyzed.

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[44]			
Units: Percentage of participants				
Visit 5 (Month 12), n=234	18			
Visit 8 (Month 24), n=166	17			
Visit 11 (Month 36), n=121	21			
Visit 14 (Month 48), n=104	19			
Visit 17 (Month 60), n=88	19			
Visit 20 (Month 72), n=58	24			
Visit 23 (Month 84), n=32	34			
Visit 26 (Month 96), n=26	35			
Visit 29 (Month 108), n=13	38			
Follow up visit, n=260	27			

Notes:

[44] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with Abnormal Results of Neurological Examination

End point title	Percentage of participants with Abnormal Results of Neurological Examination ^[45]
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End point description:

A complete neurological examination was performed at the end of each 12 month study cycle (i.e., first year, second year, third year, etc.) during the Open-Label Treatment Phase. Abnormal results were categorized as Abnormal-Not Clinically Significant (A-NCS) and Abnormal and Clinically Significant (A-CS). Only data for abnormal values on neurological examination have been presented. Only those participants available at the specified time points were analyzed.

End point type	Primary
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End point timeframe:

Baseline and up to 122 months

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			
Subject group type	Reporting group			
Number of subjects analysed	376 ^[46]			
Units: Percentage of participants				
Visit 1 (Month 1), A-NCS, n=356	23			
Visit 1 (Month 1), A-CS, n=356	10			
Visit 2 (Month 3), A-NCS, n=328	23			
Visit 2 (Month 3), A-CS, n=328	9			
Visit 3 (Month 6), A-NCS, n=287	22			
Visit 3 (Month 6), A-CS, n=287	10			
Visit 4 (Month 9), A-NCS, n=252	23			
Visit 4 (Month 9), A-CS, n=252	11			
Visit 5 (Month 12), A-NCS, n=234	27			

Visit 5 (Month 12), A-CS, n=234	12			
Visit 6 (Month 16), A-NCS, n=202	24			
Visit 6 (Month 16), A-CS, n=202	9			
Visit 7 (Month 20), A-NCS, n=179	25			
Visit 7 (Month 20), A-CS, n=179	9			
Visit 8 (Month 24), A-NCS, n=166	34			
Visit 8 (Month 24), A-CS, n=166	10			
Visit 9 (Month 28), A-NCS, n=146	32			
Visit 9 (Month 28), A-CS, n=146	8			
Visit 10 (Month 32), A-NCS, n=127	32			
Visit 10 (Month 32), A-CS, n=127	8			
Visit 11 (Month 36), A-NCS, n=121	35			
Visit 11 (Month 36), A-CS, n=121	8			
Visit 12 (Month 40), A-NCS, n=112	28			
Visit 12 (Month 40), A-CS, n=112	10			
Visit 13 (Month 44), A-NCS, n=105	31			
Visit 13 (Month 44), A-CS, n=105	9			
Visit 14 (Month 48), A-NCS, n=104	28			
Visit 14 (Month 48), A-CS, n=104	11			
Visit 15 (Month 52), A-NCS, n=91	31			
Visit 15 (Month 52), A-CS, n=91	9			
Visit 16 (Month 56), A-NCS, n=77	32			
Visit 16 (Month 56), A-CS, n=77	9			
Visit 17 (Month 60), A-NCS, n=89	29			
Visit 17 (Month 60), A-CS, n=89	9			
Visit 18 (Month 64), A-NCS, n=58	29			
Visit 18 (Month 64), A-CS, n=58	10			
Visit 19 (Month 68), A-NCS, n=53	36			
Visit 19 (Month 68), A-CS, n=53	9			
Visit 20 (Month 72), A-NCS, n=59	41			
Visit 20 (Month 72), A-CS, n=59	7			
Visit 21 (Month 76), A-NCS, n=43	40			
Visit 21 (Month 76), A-CS, n=43	7			
Visit 22 (Month 80), A-NCS, n=37	41			
Visit 22 (Month 80), A-CS, n=37	5			
Visit 23 (Month 84), A-NCS, n=32	47			
Visit 23 (Month 84), A-CS, n=32	3			
Visit 24 (Month 88), A-NCS, n=29	45			
Visit 24 (Month 88), A-CS, n=29	7			
Visit 25 (Month 92), A-NCS, n=25	40			
Visit 25 (Month 92), A-CS, n=25	8			
Visit 26 (Month 96), A-NCS, n=26	42			
Visit 26 (Month 96), A-CS, n=26	15			
Visit 27 (Month 100), A-NCS, n=19	21			
Visit 27 (Month 100), A-CS, n=19	16			
Visit 28 (Month 104), A-NCS, n=17	24			
Visit 28 (Month 104), A-CS, n=17	24			
Visit 29 (Month 108), A-NCS, n=13	31			
Visit 29 (Month 108), A-CS, n=13	8			
Follow up visit, A-NCS, n=263	22			
Follow up visit, A-CS, n=263	8			

Notes:

[46] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with retinal pigmentary abnormalities (RPA)

End point title	Percentage of participants with retinal pigmentary abnormalities (RPA)
End point description: RPA was determined by either an ophthalmologist or retina specialist. RPA is the composite endpoint assessed by its components: pigmentary abnormalities (PA) in the macula, PA in the peripheral retina (PR), PA in both macula and PR and PA at location unspecified. Only those participants with ≥ 1 ophthalmology exam on or before last dose of retigabine are presented..	
End point type	Secondary
End point timeframe: Up to 121 months	

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	54 ^[47]			
Units: Percentage of participants				
RPA	31			
PA in the macula	22			
PA of the PR	22			
PA in both the macula and PR	13			
PA: location unspecified	2			

Notes:

[47] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with pigmentation of non-retinal ocular tissue (Non-ret. Pig. Abn)

End point title	Percentage of participants with pigmentation of non-retinal ocular tissue (Non-ret. Pig. Abn)
End point description: Non-retinal ocular tissue abnormalities were determined by either an ophthalmologist or retina specialist. Non-ret. Pig. Abn is a composite endpoint assessed by its components: abnormal pigmentation (ABP) of the sclera and/or conjunctiva, ABP of the cornea, ABP of the iris and ABP of the lens. Only those participants with ≥ 1 ophthalmology exam on or before last dose of retigabine are presented.	
End point type	Secondary

End point timeframe:

Up to 121 months

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	54 ^[48]			
Units: Percentage of participants				
Non-ret. Pig. Abn	28			
ABP of sclera and/or conjunctiva	13			
ABP of the cornea	4			
ABP of the iris	17			
ABP of the lens	0			

Notes:

[48] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with abnormal pigmentation of skin, including the skin around the eyes and the eyelids, lips, nails, or mucosa

End point title	Percentage of participants with abnormal pigmentation of skin, including the skin around the eyes and the eyelids, lips, nails, or mucosa
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End point description:

Abnormal discoloration of the skin was determined by a dermatologist. The parameters assessed were abnormal discoloration of the skin, abnormal discoloration of the lips, abnormal discoloration of the nails, abnormal discoloration of the mucosa, abnormal discoloration of sun-exposed tissue, abnormal discoloration of non sun-exposed tissue. Only those participants with at least one skin exam by the investigator or dermatologist on or before the last dose of retigabine or dermatologist-confirmed discoloration with start date on or before the date of last dose of retigabine are presented.

End point type	Secondary
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End point timeframe:

Up to 121 months

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	46 ^[49]			
Units: Percentage of participants				
Any abnormal dermatologic discoloration	50			
Abnormal discoloration of lips	26			
Abnormal discoloration of skin	37			
Abnormal discoloration of nails	41			
Abnormal discoloration of mucosa	30			
Abnormal discoloration of sun-exposed tissue	48			

Abnormal discoloration of non sun-exposed tissue	37			
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Notes:

[49] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a clinically significant decrease (CSD) in visual acuity (VA) from initial examination

End point title	Percentage of participants with a clinically significant decrease (CSD) in visual acuity (VA) from initial examination
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End point description:

VA refers to the clarity of vision. The parameters assessed were CSD in VA from initial examination which can be explained and CSD in VA from initial examination which cannot be explained. Only those participants with both initial and at least 1 follow-up exam while on retigabine are presented.

End point type	Secondary
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End point timeframe:

Up to 121 months

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	38 ^[50]			
Units: Percentage of participants				
CSD in VA from initial examination, n=38	13			
CSD which can be explained (Form 2), n=34	12			
CSD which can not be explained (Form 2), n=34	0			

Notes:

[50] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with decrease in confrontational visual field from initial examination

End point title	Percentage of participants with decrease in confrontational visual field from initial examination
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End point description:

The parameter assessed was decrease in confrontational visual field from initial examination. Only those participants with data available at the indicated time point were analyzed. Only those participants with both initial and at least 1 follow-up exam while on retigabine are presented.

End point type	Secondary
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End point timeframe:

Up to 121 months

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	38 ^[51]			
Units: Percentage of participants				
Percentage of participants	13			

Notes:

[51] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in the 28-day partial seizure rate from the Baseline phase (obtained during the 8-week Baseline period of Study VRX-RET-E22-302) to open-label treatment.

End point title	Percentage change in the 28-day partial seizure rate from the Baseline phase (obtained during the 8-week Baseline period of Study VRX-RET-E22-302) to open-label treatment.
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End point description:

28-day partial seizure rate observed during the OLE period was compared to the 28-day partial seizure rate observed during the Baseline phase of the double-blind parent study VRX-R ET-E22-302. Percent change from Baseline in 28-day total partial seizure rate was calculated as ([28-day partial seizure frequency for the period of interest – Baseline 28-day partial seizure frequency] / Baseline 28-day partial seizure frequency) × 100 percent. A negative percent change indicated a reduction (improvement) from Baseline, so the best possible outcome was -100 percent. Only those participants with data available at the indicated time point were analyzed.

End point type	Secondary
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End point timeframe:

Baseline and up to 121 months

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	371 ^[52]			
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change	-36.1 (± 95.77)			

Notes:

[52] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with 50% Reduction in Seizure Frequency From Baseline Phase of the Parent Study (VRX-RET-E22-302) to Open Label Treatment

End point title	Percentage of Participants with 50% Reduction in Seizure Frequency From Baseline Phase of the Parent Study (VRX-RET-E22-302) to Open Label Treatment
End point description: A Responder was defined as a participant with ≥ 50 percent decrease from Baseline in the 28-day partial seizure frequency, i.e., a percent change from Baseline less than or equal to -50 percent. The percentage of responders from Baseline phase of the parent study (VRX-RET-E22-302) to open label treatment have been presented.	
End point type	Secondary
End point timeframe: Baseline and up to 121 months	

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	371 ^[53]			
Units: Percentage of participants				
Percentage of responders	52			

Notes:

[53] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who were seizure free for any 6 continuous months

End point title	Number of participants who were seizure free for any 6 continuous months
End point description: Seizure free for any continuous 6 months is defined as no seizures occurring during any consecutive 180 days between the first date (Baseline) and the last date (before tapering of dose). The number of participants who were seizure free for 6 continuous months within the 121 month OLE period have been presented.	
End point type	Secondary
End point timeframe: Up to 6 continuous months within the 121 months period	

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	279 ^[54]			
Units: Participants				
Participants	36			

Notes:

[54] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who were seizure free for any 12 continuous months

End point title	Number of participants who were seizure free for any 12 continuous months
End point description: Seizure free for any continuous 12 months is defined as no seizures occurring during any consecutive 360 days. Number of participants who were seizure free for 12 continuous months within the 121 month OLE period have been presented.	
End point type	Secondary
End point timeframe: Up to 12 continuous months within the 121 months period	

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	222 ^[55]			
Units: Participants				
Participants	22			

Notes:

[55] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of seizure free days

End point title	Percentage of seizure free days
End point description: A seizure free day is defined as the number of applicable days without any seizures (partial, generalized or unclassified). Only the days in which a subject had non-missing seizure data were considered as applicable days. Percentage of seizure free days is calculated as Number of seizure free days / number of applicable days × 100 percent. Only those participants with data available at the indicated time point were analyzed.	
End point type	Secondary
End point timeframe: Up to 121 months	

End point values	Retigabine			
Subject group type	Reporting group			
Number of subjects analysed	371 ^[56]			
Units: Percentage of days				
arithmetic mean (standard deviation)				
Percentage of days	76.8 (± 26.11)			

Notes:

[56] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of the study treatment upto 122 months

Adverse event reporting additional description:

Safety population was used to assess AEs and SAEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Retigabine
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Reporting group description:

Eligible participants entered a 4-week transition phase of the double-blind parent study (study VRX-RET-E22-302), in which their dose of retigabine was titrated to or maintained at 300 mg three times daily (900 mg per day). Upon completion of the Transition phase of the parent study, participants enrolled into the extension study (RTG115097). Once enrolled in the OLE, doses were adjusted within the range of 600 mg to 1200 mg per day as an adjunct therapy to their ongoing AEDs with or without VNS up to 121 months.

Serious adverse events	Retigabine		
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 376 (20.74%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphoma			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Plasma cell myeloma			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Uterine leiomyoma			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Tracheostomy			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden unexplained death in epilepsy			

subjects affected / exposed	3 / 376 (0.80%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	2 / 3		
Chest pain			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Treatment noncompliance			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 376 (0.53%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	4 / 376 (1.06%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	3 / 376 (0.80%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Psychogenic seizure			
subjects affected / exposed	2 / 376 (0.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Aggression				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Agitation				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epileptic psychosis				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination, auditory				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucinations, mixed				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Obsessive-compulsive personality disorder				

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postictal psychosis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burns second degree			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burns third degree			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			

subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Near drowning				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skull fractured base			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Seizure			
subjects affected / exposed	16 / 376 (4.26%)		
occurrences causally related to treatment / all	6 / 23		
deaths causally related to treatment / all	0 / 0		
Epilepsy			

subjects affected / exposed	6 / 376 (1.60%)			
occurrences causally related to treatment / all	4 / 7			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	5 / 376 (1.33%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	5 / 376 (1.33%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	3 / 376 (0.80%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Focal dyscognitive seizures				
subjects affected / exposed	3 / 376 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Coma				
subjects affected / exposed	2 / 376 (0.53%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Arachnoid cyst				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ataxia				
subjects affected / exposed	1 / 376 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depressed level of consciousness			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysarthria			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Facial paralysis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incoherent			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Partial seizures			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Partial seizures with secondary generalisation			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure cluster			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal pigmentation			
subjects affected / exposed	3 / 376 (0.80%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Diplopia			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vision blurred			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pigmentation disorder			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephropathy toxic			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Gastroenteritis			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia streptococcal			

subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Typhoid fever			
subjects affected / exposed	1 / 376 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 376 (0.53%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Retigabine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	239 / 376 (63.56%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	83 / 376 (22.07%)		
occurrences (all)	140		
Somnolence			
subjects affected / exposed	78 / 376 (20.74%)		
occurrences (all)	99		
Headache			
subjects affected / exposed	61 / 376 (16.22%)		
occurrences (all)	231		
Tremor			
subjects affected / exposed	34 / 376 (9.04%)		
occurrences (all)	42		

Memory impairment subjects affected / exposed occurrences (all)	26 / 376 (6.91%) 31		
Seizure subjects affected / exposed occurrences (all)	22 / 376 (5.85%) 37		
Aphasia subjects affected / exposed occurrences (all)	20 / 376 (5.32%) 27		
Amnesia subjects affected / exposed occurrences (all)	19 / 376 (5.05%) 23		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	43 / 376 (11.44%) 50		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	19 / 376 (5.05%) 19		
Gastrointestinal disorders Oral mucosal discolouration subjects affected / exposed occurrences (all)	20 / 376 (5.32%) 23		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	22 / 376 (5.85%) 25		
Infections and infestations Viral upper respirator tract infection subjects affected / exposed occurrences (all)	30 / 376 (7.98%) 45		
Influenza subjects affected / exposed occurrences (all)	24 / 376 (6.38%) 42		
Urinary tract infection			

subjects affected / exposed	21 / 376 (5.59%)		
occurrences (all)	25		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2007	• A urine pregnancy test at Visit 0, for female participants, was added. • Pregnancy exclusion criteria were more clearly defined. • Modifications of dosage scheduling were allowed and defined for the investigator. • Interim study visits were added to allow more frequent haematological monitoring per Food and Drug Administration (FDA) comment. • Expedited reporting of low neutrophil counts and discontinuation due to haematological reasons or infections was added per FDA comment.
14 August 2008	• Extended the study from 36 to 48 months • American Urological Association (AUA) and post-void residual (PVR) assessments added at the end of second, third and fourth year of this study at Visits 8, 11 and 14. • Full physical and neurological examination to be performed at Visit 14 and brief neurological examinations added at Visits 12 and 13. • Added a 12-lead ECG at Visit 14. • Participants tapering/discontinuing in the fourth year, were to complete assessments and evaluations scheduled for Visit 14.
10 March 2010	• Visits X, Y, Z were added to enable an open ended visit schedule. Study Visit_X, Study Visit_Y and Study Visit _Z/Early Termination occurred in 4 month intervals and designated additional 12-month periods after the participant had completed Visit 14 in the study. Once the participant had completed Study V_Z/Early Termination, they repeated Study V_X at the next scheduled visit and entered into the subsequent 12 month cycle. This continued for each 12-month period, providing an open-ended visit schedule, which allowed participant to remain on treatment until the study drug, retigabine, was approved and commercially available, or until the program was discontinued. • Information on when participant were to return for the final visit after discontinuation was clarified as 1 to 30 days following their last dose intake of study drug.
08 March 2011	• Ownership of retigabine and sponsorship of the study were transferred from Valeant Pharmaceuticals International, Inc to GSK • From this amendment, retigabine was supplied by GSK.
03 November 2011	• Updated Quintiles address • Clarified there was to be a 3-week tapering period for participant who withdrew from the study prematurely • Clarified that the 30-day post-study period for collection of AEs was for all subjects • Added participant switched to commercially available retigabine as a reason for withdrawal and included information on how to switch participant to commercially available retigabine.
11 December 2012	• Included the option to continue retigabine in another long-term study if this study was discontinued by the Sponsor if the subject was expected to benefit from continued treatment. • All participant were referred to an ophthalmologist for baseline eye examinations and annual eye examinations included in the study procedures. • If a participant withdrew from the study early, an eye examination was to be performed if it had been greater than 6 months since their last examination. • Any participant with discolouration/pigmentation of nail, skin and/or mucosal surfaces were referred to a dermatologist who completed the Targeted Follow-up Questionnaire.

06 November 2013	• Included an additional secondary objective to evaluate whether retinal pigmentation, unexplained vision loss, pigmentation of non-retinal ocular tissue (NROT) and discolouration of nails (DON), lips, skin or mucosa change over time after discontinuation of retigabine. • Removed the option to continue retigabine in another long-term open-label safety study; requirement to transition participants to commercial retigabine when available was removed (made optional). • The study design was modified to include a SFUCP for eligible participants. • Added the new assessments (comprehensive eye and dermatological examination) and 2 analysis phases (primary and final completion) to allow for reporting after the end of the Open-Label/Safety Follow-up Phase and after the end of the overall study. • Follow-up comprehensive skin and eye examinations were collected for participants who previously discontinued retigabine. • Details on procedures to be carried out during the SFUCP were added. • Additional reasons for withdrawal from the Open-Label Treatment Phase/ study were added which included occurrence of any of the following events: agranulocytosis, anaphylaxis and anaphylactoid reactions, hepatotoxicity, acute renal failure, Stevens Johnson Syndrome/Toxic Epidermal Necrolysis, actual/risk of suicide attempt, status epilepticus in a participant who does not have a history of previous episodes of status epilepticus/risk of retinal pigmentation and possible associated vision loss that outweighs the benefits of continued treatment with retigabine for participants who have other suitable treatment options. • The following were designated adverse events of special interest (AESIs): RPA and/or vision loss (e.g., decrease in visual acuity and/visual field), pigmentation of NROT (conjunctiva, sclera, iris) DON, lips, skin, and mucosa. • Added Appendix E for the plan to collect an optional blood sample for potential pharmacogenetic (PGx) analysis in participants on treatment/SFUCP.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported