Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study to Evaluate the Efficacy and Safety of VX-765 in Subjects With Treatment-Resistant Partial Epilepsy With a 24-Week Open-Label Extension

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-004156-19
Trial protocol	DE CZ AT HU GB FI
Global end of trial date	24 September 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	13 July 2016

Trial information

Trial identification

Sponsor protocol code	VX11-765-402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01501383
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part A: To evaluate the efficacy of VX-765 to treat seizures in subjects with treatment-resistant partial epilepsy and to evaluate the safety and tolerability of VX-765 in subjects with treatment-resistant partial epilepsy; Part B: To evaluate the safety and tolerability of long term VX-765 treatment in subjects with treatment-resistant partial epilepsy.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	55
EEA total number of subjects	7

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)	55
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

An administrative decision was made by Vertex Pharmaceuticals Incorporated (Vertex) to stop the enrollment of subjects during the conduct of this study and to postpone further clinical development of VX-765 for the treatment of epilepsy. A total of 55 subjects were randomized in to study.

Period 1

Period 1 title	Part A: Double Blind Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Placebo

Arm description:

Placebo matched to VX-765 tablet three times daily (TID) up to Week 13.

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

Dosage and administration details:

Placebo matched to VX-765 tablet TID.

Arm title	Part A VX-765 300 mg

Arm description:

VX-765 300 milligram(mg) tablet TID up to Week 13.

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Arm title	Part A VX-765 600 mg

Arm description:

VX-765 600 mg tablet TID up to Week 13.

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: VX-765 tablet TID.

Arm title	Part A VX-765 900 mg
Arm description: VX-765 900 mg tablet TID up to Week 13.	
Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: VX-765 tablet TID.	

Arm title	Part A VX-765 1200 mg
Arm description: VX-765 1200 mg tablet TID up to Week 13.	
Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: VX-765 1200 mg tablet TID.	

Number of subjects in period 1	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg
Started	12	10	11
Completed	10	8	11
Not completed	2	2	0
Consent withdrawn by subject	-	-	-
Adverse Events	2	2	-
Subject Refused Further Dosing (Not Due to AE)	-	-	-

Number of subjects in period 1	Part A VX-765 900 mg	Part A VX-765 1200 mg
Started	11	11
Completed	9	11
Not completed	2	0
Consent withdrawn by subject	1	-
Adverse Events	-	-
Subject Refused Further Dosing (Not Due to AE)	1	-

Period 2

Period 2 title	Part B: Open-label Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Placebo to Part B VX-765 600/900/1200 mg

Arm description:

Subjects who received placebo matched to VX-765 tablet (TID) up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Arm title	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg

Arm description:

Subjects who received VX-765 300 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Arm title	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg

Arm description:

Subjects who received VX-765 600 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Arm title	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg

Arm description:

Subjects who received VX-765 900 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Arm title	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg

Arm description:

Subjects who received VX-765 1200 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).

Arm type	Experimental
Investigational medicinal product name	VX-765
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

VX-765 tablet TID.

Number of subjects in period 2[1]	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg
Started	10	8	9
Completed	6	7	7
Not completed	4	1	2
Physician Decision	1	-	-
Subject Withdrew Consent	-	1	1
Adverse Events	2	-	1
Subject Refused Further Dosing (Not Due to AE)	1	-	-

Number of subjects in period 2[1]	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg
Started	9	10
Completed	8	6
Not completed	1	4
Physician Decision	1	1
Subject Withdrew Consent	-	-

Adverse Events	-	1
Subject Refused Further Dosing (Not Due to AE)	-	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only subjects who completed the Part A Treatment Period and elected to enter Part B and met Part B eligibility criteria were included in Part B.

Baseline characteristics

Reporting groups	
Reporting group title	Part A Placebo
Reporting group description:	
Placebo matched to VX-765 tablet three times daily (TID) up to Week 13.	
Reporting group title	Part A VX-765 300 mg
Reporting group description:	
VX-765 300 milligram(mg) tablet TID up to Week 13.	
Reporting group title	Part A VX-765 600 mg
Reporting group description:	
VX-765 600 mg tablet TID up to Week 13.	
Reporting group title	Part A VX-765 900 mg
Reporting group description:	
VX-765 900 mg tablet TID up to Week 13.	
Reporting group title	Part A VX-765 1200 mg
Reporting group description:	
VX-765 1200 mg tablet TID up to Week 13.	

Reporting group values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg
Number of subjects	12	10	11
Age categorical Units: Subjects			

Age continuous			
Due to EudraCT limitations, it is not possible to report Mean (SD) for total column.			
Units: years			
arithmetic mean	43.3	35.2	37.6
standard deviation	± 12.26	± 14.27	± 10.03
Gender categorical Units: Subjects			
Female	6	6	5
Male	6	4	6

Reporting group values	Part A VX-765 900 mg	Part A VX-765 1200 mg	Total
Number of subjects	11	11	55
Age categorical Units: Subjects			

Age continuous			
Due to EudraCT limitations, it is not possible to report Mean (SD) for total column.			
Units: years			
arithmetic mean	35.4	40.7	
standard deviation	± 10.58	± 13.75	-
Gender categorical Units: Subjects			
Female	4	6	27
Male	7	5	28

End points

End points reporting groups

Reporting group title	Part A Placebo
Reporting group description:	
Placebo matched to VX-765 tablet three times daily (TID) up to Week 13.	
Reporting group title	Part A VX-765 300 mg
Reporting group description:	
VX-765 300 milligram(mg) tablet TID up to Week 13.	
Reporting group title	Part A VX-765 600 mg
Reporting group description:	
VX-765 600 mg tablet TID up to Week 13.	
Reporting group title	Part A VX-765 900 mg
Reporting group description:	
VX-765 900 mg tablet TID up to Week 13.	
Reporting group title	Part A VX-765 1200 mg
Reporting group description:	
VX-765 1200 mg tablet TID up to Week 13.	
Reporting group title	Part A Placebo to Part B VX-765 600/900/1200 mg
Reporting group description:	
Subjects who received placebo matched to VX-765 tablet (TID) up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).	
Reporting group title	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg
Reporting group description:	
Subjects who received VX-765 300 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).	
Reporting group title	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg
Reporting group description:	
Subjects who received VX-765 600 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).	
Reporting group title	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Reporting group description:	
Subjects who received VX-765 900 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).	
Reporting group title	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg
Reporting group description:	
Subjects who received VX-765 1200 mg tablet TID up to Week 13 in Part A and met Part B eligibility criteria, received VX-765 900 mg TID for 12 weeks (from end of Week 13 through Week 25) followed by VX-765 600 mg or 900 mg or 1200 mg as per Investigator discretion for 12 weeks (Week 26 through Week 37).	

Primary: Part A: Percent Reduction in Weekly Seizure Frequency During Part A Late Treatment Period Compared to Part A Baseline

End point title	Part A: Percent Reduction in Weekly Seizure Frequency During Part A Late Treatment Period Compared to Part A Baseline

End point description:

Percent reduction in weekly seizure frequency refers to the percent reduction in the (average) weekly seizure frequency occurring during a target time period relative to the Baseline Period in Part A. Seizure frequency was derived from observed seizure frequency data by normalizing the observed data to a 7-day period, with no imputation for gaps in reporting or early discontinuations. Analysis was performed on Part A Full Analysis Set (FAS) (defined as all randomized subjects who received at least 1 dose of study drug [VX-765 or placebo] and had at least 1 treatment-period efficacy measurement) subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 5 to Week 9), in each treatment group.

End point type	Primary

End point timeframe:

Part A baseline, Part A late treatment period (Week 5 through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	11	10
Units: percent change				
median (confidence interval 95%)	-3.63 (-37.77 to 20.8)	-13.64 (-45.91 to 18.18)	-14.06 (-42.07 to -2.41)	16.16 (-27.96 to 102.41)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percent change				
median (confidence interval 95%)	-25.3 (-58.88 to 1.71)			

Statistical analyses

Statistical analysis title	Jonckheere-Terpstra Trend Comparison
Comparison groups	Part A Placebo v Part A VX-765 300 mg v Part A VX-765 600 mg v Part A VX-765 900 mg v Part A VX-765 1200 mg
Number of subjects included in analysis	51
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.5223
Method	Jonckheere-Terpstra Trend Test

Primary: Part A: Percentage of Subjects with 50% or Greater Reduction in Weekly

Seizure Frequency During Part A Late Treatment Period Compared to Part A Baseline

End point title	Part A: Percentage of Subjects with 50% or Greater Reduction in Weekly Seizure Frequency During Part A Late Treatment Period Compared to Part A Baseline

End point description:

The 95% confidence interval (CI) examine the >=50% response rate proportion CI for each treatment group, separately. This test served as an additional method (unadjusted by baseline seizure frequency) to examine the proportions of subjects with >=50% reduction in seizure frequency during the Late Treatment Period. Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 5 to Week 9), in each treatment group.

End point type	Primary

End point timeframe:

Part A baseline, Part A late treatment period (Week 5 through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	11	10
Units: percentage of subjects				
number (confidence interval 95%)	20 (2.5 to 55.6)	22.2 (2.8 to 60)	27.3 (6 to 61)	0 (0 to 30.9)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percentage of subjects				
number (confidence interval 95%)	36.4 (10.9 to 69.2)			

Statistical analyses

Statistical analysis title	Cochran Armitage Trend Test

Statistical analysis description:

P value for linear trend test between the placebo group and the 4 sequentially dose-escalated VX-765 treatment groups.

Comparison groups	Part A Placebo v Part A VX-765 300 mg v Part A VX-765 600 mg v Part A VX-765 900 mg v Part A VX-765 1200 mg
Number of subjects included in analysis	51
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.8147
Method	Cochran Armitage Trend Test

Primary: Part A: Safety and Tolerability – Percentage of Subjects with Adverse

Events (AEs) and Serious Adverse Events (SAEs)

End point title	Part A: Safety and Tolerability – Percentage of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

Treatment-emergent AEs (TEAEs), referred to as AEs, for Part A were defined as any AEs that were reported or worsened on or after the start of study drug (1) through the Part A Safety Follow-up Visit for subjects who were not eligible or did not elect to enter the OLE, and (2) through the last day of the Part A Treatment Period for subjects who entered the OLE. Results are reported separately for treatment period (TP) and safety follow-up period (SFUP). The Safety Set for Part A included all subjects who received at least 1 dose of study drug. The number of subjects for each time-point are specified as "n".

End point type	Primary

End point timeframe:

Part A: Start of study drug through safety follow-up (up to Week 17)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for safety endpoint.

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	11	11
Units: percentage of subjects				
number (not applicable)				
TP: Subjects with AEs (n = 12, 10, 11, 11, 11)	83.3	50	72.7	54.5
TP: Subjects with SAEs (n = 12, 10, 11, 11, 11)	0	0	9.1	0
SFUP: Subjects with AEs (n = 2, 2, 2, 2, 1)	50	100	50	0
SFUP: Subjects with SAEs (n = 2, 2, 2, 2, 1)	50	0	0	0

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percentage of subjects				
number (not applicable)				
TP: Subjects with AEs (n = 12, 10, 11, 11, 11)	72.2			
TP: Subjects with SAEs (n = 12, 10, 11, 11, 11)	0			
SFUP: Subjects with AEs (n = 2, 2, 2, 2, 1)	0			
SFUP: Subjects with SAEs (n = 2, 2, 2, 2, 1)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Safety and Tolerability – Percentage of Subjects with AEs and SAEs

End point title	Part B: Safety and Tolerability – Percentage of Subjects with AEs and SAEs[2]

End point description:

TEAEs for Part B were defined as AEs that were reported or worsened on or after the start of Part B study drug dosing through the Part B Safety Follow-up Visit. Results are reported separately for treatment period (TP) and safety follow-up period (SFUP). The Safety Set for Part B included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Part B: Start of study drug through safety follow-up (up to Week 41)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for safety endpoint.

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	7	8	9
Units: percentage of subjects				
number (not applicable)				
TP: Subjects with AEs	80	71.4	87.5	77.8
TP: Subjects with SAEs	10	0	0	0
SFUP: Subjects with AEs	10	57.1	37.5	11.1
SFUP: Subjects with SAEs	0	14.3	12.5	0

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of subjects				
number (not applicable)				
TP: Subjects with AEs	66.7			
TP: Subjects with SAEs	0			
SFUP: Subjects with AEs	11.1			
SFUP: Subjects with SAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects Who Were Seizure-Free During the Part A Late Treatment Period

End point title	Part A: Percentage of Subjects Who Were Seizure-Free During the Part A Late Treatment Period

End point description:

Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 5 to Week 9), in each treatment group.

End point type	Secondary

End point timeframe:

Part A late treatment period (Week 5 through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	11	10
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 30.9)	11.1 (0.3 to 48.3)	0 (0 to 28.5)	0 (0 to 30.9)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 28.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percent Reduction in Weekly Seizure Frequency During Entire Part A Treatment Period Compared to Part A Baseline

End point title	Part A: Percent Reduction in Weekly Seizure Frequency During Entire Part A Treatment Period Compared to Part A Baseline

End point description:

Percent reduction in weekly seizure frequency refers to the percent reduction in the (average) weekly seizure frequency occurring during a target time period relative to the Baseline Period in Part A. Seizure frequency was derived from observed seizure frequency data by normalizing the observed data to a 7-day period, with no imputation for gaps in reporting or early discontinuations. Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 1 to Week 7), in each treatment group.

End point type	Secondary

End point timeframe:

Part A baseline, Part A entire treatment period (through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	11	11
Units: percent change				
median (confidence interval 95%)	-1.48 (-25.61 to 21.9)	-0.16 (-40.74 to 20.89)	-10.33 (-35.84 to 2.54)	17.06 (-13.97 to 67.59)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percent change				
median (confidence interval 95%)	-5.64 (-50.22 to 6.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects with 50% or Greater Reduction in Weekly Seizure Frequency During Part A Entire Treatment Period Compared to Part A Baseline

End point title	Part A: Percentage of Subjects with 50% or Greater Reduction in Weekly Seizure Frequency During Part A Entire Treatment Period Compared to Part A Baseline

End point description:

Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 1 to Week 7), in each treatment group.

End point type	Secondary

End point timeframe:

Part A baseline, Part A entire treatment period (through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	11	11
Units: percentage of subjects				
number (confidence interval 95%)	18.2 (2.3 to 51.8)	11.1 (0.3 to 48.3)	9.1 (0.2 to 41.3)	0 (0 to 28.5)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			

Units: percentage of subjects				
number (confidence interval 95%)	36.4 (10.9 to 69.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Subjects Who Were Seizure-Free During the Part A Entire Treatment Period

End point title	Part A: Percentage of Subjects Who Were Seizure-Free During the Part A Entire Treatment Period

End point description:

Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 1 to Week 7), in each treatment group.

End point type	Secondary

End point timeframe:

Part A entire treatment period (through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	11	11
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 28.5)	0 (0 to 33.6)	0 (0 to 28.5)	0 (0 to 28.5)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 28.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Maximum Number of Consecutive Days that Subjects did not have Seizures at any time During the Part A Late Treatment Period

End point title	Part A: Maximum Number of Consecutive Days that Subjects did not have Seizures at any time During the Part A Late Treatment Period

End point description:

Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 5 to Week 9), in each treatment group.

End point type	Secondary

End point timeframe:

Part A late treatment period (Week 5 through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	11	10
Units: days				
arithmetic mean (standard deviation)	10.6 (± 11.26)	13.3 (± 19.59)	12.2 (± 7.57)	9.8 (± 5.73)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: days				
arithmetic mean (standard deviation)	12.2 (± 9.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Maximum Number of Consecutive Days that Subjects did not have Seizures at any time During the Part A Entire Treatment Period

End point title	Part A: Maximum Number of Consecutive Days that Subjects did not have Seizures at any time During the Part A Entire Treatment Period

End point description:

Analysis was performed on Part A FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 1 to Week 7), in each treatment group.

End point type	Secondary

End point timeframe:

Part A entire treatment period (through Week 13)

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	11	11
Units: days				
arithmetic mean (standard deviation)	10.7 (± 12.38)	15.7 (± 25.98)	12.9 (± 7.49)	12 (± 7.4)

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: days				
arithmetic mean (standard deviation)	12.5 (± 9.66)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of VX-765, VRT-043198, and Concomitant Antiepileptic Drug (AED) Levels in blood

End point title	Pharmacokinetics (PK) of VX-765, VRT-043198, and Concomitant Antiepileptic Drug (AED) Levels in blood

End point description:

The PK analyses are omitted per the FDA Guidance Document "Submission of Abbreviated Reports and Synopses in Support of Marketing Applications".

End point type	Secondary

End point timeframe:

NA

End point values	Part A Placebo	Part A VX-765 300 mg	Part A VX-765 600 mg	Part A VX-765 900 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: NA				

Notes:

[3] - The PK analyses are omitted as specified in endpoint description.

[4] - The PK analyses are omitted as specified in endpoint description.

[5] - The PK analyses are omitted as specified in endpoint description.

[6] - The PK analyses are omitted as specified in endpoint description.

End point values	Part A VX-765 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: NA				

Notes:

[7] - The PK analyses are omitted as specified in endpoint description.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point title	Part B: Percent Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point description:

Percent reduction in weekly seizure frequency refers to the percent reduction in the (average) weekly seizure frequency occurring during a target time period relative to the Baseline Period in Part A. Seizure frequency was derived from observed seizure frequency data by normalizing the observed data to a 7-day period, with no imputation for gaps in reporting or early discontinuations. Analysis was performed on Part B FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 14 to Week 25), in each treatment group.

End point type	Secondary

End point timeframe:

Part A Baseline, Part B entire treatment period (end of Week 13 through Week 37)

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	9
Units: percent change				
arithmetic mean (standard deviation)	-15.04 (± 30.386)	-33.27 (± 46.353)	-11.21 (± 31.476)	14.28 (± 47.684)

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percent change				
arithmetic mean (standard deviation)	-21.26 (± 38.954)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Subjects with 50% or Greater Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point title	Part B: Percentage of Subjects with 50% or Greater Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point description:

Analysis was performed on Part B FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 14 to Week 25), in each treatment group.

End point type	Secondary

End point timeframe:

Part A Baseline, Part B entire treatment period (end of Week 13 through Week 37)

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	9
Units: percentage of subjects				
number (confidence interval 95%)	22.2 (0 to 49.4)	42.9 (6.2 to 79.5)	25 (0 to 55)	0 (0 to 0)

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of subjects				
number (confidence interval 95%)	25 (0 to 55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with 75% or Greater Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point title	Percentage of Subjects with 75% or Greater Reduction in Weekly Seizure Frequency During Part B Entire Treatment Period Compared to Part A Baseline

End point description:

End point type	Secondary

End point timeframe:

Part A Baseline, Part B entire treatment period (end of Week 13 through Week 37)

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	0[11]
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[8] - Analysis was not performed due to early study termination.

[9] - Analysis was not performed due to early study termination.

[10] - Analysis was not performed due to early study termination.

[11] - Analysis was not performed due to early study termination.

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[12] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Subjects Who Were Seizure-Free During the Part B Entire Treatment Period

End point title	Part B: Percentage of Subjects Who Were Seizure-Free During the Part B Entire Treatment Period

End point description:

Analysis was performed on Part B FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 14 to Week 25), in each treatment group.

End point type	Secondary

End point timeframe:

Part B entire treatment period (end of Week 13 through Week 37)

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	9
Units: percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Subjects in Categories of Total Number of Days Seizure-free During the Part B Entire Treatment Period

End point title	Part B: Number of Subjects in Categories of Total Number of Days Seizure-free During the Part B Entire Treatment Period

End point description:

Number of subjects are reported in categories of total number of days seizure-free. Analysis was performed on Part B FAS subjects who met the minimum seizure-log data criteria of at least half of the time period (Week 14 to Week 25), in each treatment group.

End point type	Secondary

End point timeframe:

Part B entire treatment period (end of Week 13 through Week 37)

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	7	8	9
Units: number of subjects				
>=150 Days	0	3	0	1
>=120 Days	4	5	3	4
>=100 Days	4	5	6	5
>=90 Days	4	6	6	7

>=80 Days	5	6	6	7
>=70 Days	5	6	7	7
>=60 Days	7	6	7	8
>=50 Days	7	6	7	8
>=40 Days	7	6	8	8
>=30 Days	8	6	8	8
>=20 Days	8	6	8	8
>=10 Days	9	6	8	8
>0 Days	9	7	8	9
0 Days	0	0	0	0

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: number of subjects				
>=150 Days	2			
>=120 Days	4			
>=100 Days	5			
>=90 Days	5			
>=80 Days	5			
>=70 Days	6			
>=60 Days	7			
>=50 Days	7			
>=40 Days	7			
>=30 Days	7			
>=20 Days	7			
>=10 Days	7			
>0 Days	8			
0 Days	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Increase in Weekly Seizure-Free Days During the Part B Entire Treatment Period Compared to the Part A Baseline Period

End point title	Part B: Percent Increase in Weekly Seizure-Free Days During the Part B Entire Treatment Period Compared to the Part A Baseline Period

End point description:

End point type	Secondary

End point timeframe:

NA

End point values	Part A Placebo to Part B VX-765 600/900/1200 mg	Part A VX-765 300 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 600 mg to Part B VX-765 600/900/1200 mg	Part A VX-765 900 mg to Part B VX-765 600/900/1200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	0[14]	0[15]	0[16]
Units: NA				
number (not applicable)				

Notes:

[13] - Analysis was not performed due to early study termination.

[14] - Analysis was not performed due to early study termination.

[15] - Analysis was not performed due to early study termination.

[16] - Analysis was not performed due to early study termination.

End point values	Part A VX-765 1200 mg to Part B VX-765 600/900/1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[17]			
Units: NA				
number (not applicable)				

Notes:

[17] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Part A: Start of study drug through safety follow-up (up to Week 17); Part B: Start of study drug through safety follow-up (up to Week 41)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Placebo - Part A
Reporting group description: Placebo matched to VX-765 tablets TID up to Week 13.	
Reporting group title	VX-765 300 mg - Part A
Reporting group description: VX-765 300 mg tablet TID up to Week 13.	
Reporting group title	VX-765 600 mg - Part A
Reporting group description: VX-765 600 mg tablet TID up to Week 13.	
Reporting group title	VX-765 900 mg - Part A
Reporting group description: VX-765 900 mg tablet TID up to Week 13.	
Reporting group title	VX-765 1200 mg - Part A
Reporting group description: VX-765 1200 mg tablet TID up to Week 13.	
Reporting group title	VX-765 - Overall Part B
Reporting group description: Subjects who received any dose of VX-765 TID during Part B.	

Serious adverse events	Placebo - Part A	VX-765 300 mg - Part A	VX-765 600 mg - Part A
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 11 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Complex partial seizures			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VX-765 900 mg - Part A	VX-765 1200 mg - Part A	VX-765 - Overall Part B
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	3 / 43 (6.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Carbon monoxide poisoning			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Complex partial seizures			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo - Part A	VX-765 300 mg - Part A	VX-765 600 mg - Part A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	5 / 10 (50.00%)	8 / 11 (72.73%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiomyolipoma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			

Accelerated hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Influenza like illness			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Drug Hypersensitivity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Nasal congestion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumonia Aspiration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Sinus Congestion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Affect Lability			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dysphemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Stress			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Anxiety			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Anticonvulsant Drug Level Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Blood pressure increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Procedural Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Fall			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cartilage injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lip injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle Strain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Thermal Burn			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 12 (25.00%)	3 / 10 (30.00%)	1 / 11 (9.09%)
occurrences (all)	5	3	1
Burning Sensation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cerebellar Atrophy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Head Discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyporeflexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sedation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Convulsion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Postictal paralysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Status epilepticus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypoacusis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Diplopia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye Irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vision Blurred			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blepharospasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	5	1	0
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Dyspepsia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	2
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dry Mouth			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Frequent Bowel Movements			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia Oral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Tongue Disorder			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hepatic Function Abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Increased Tendency to Bruise			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pruritus Generalised			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Musculoskeletal Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	2
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Acute Tonsillitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Genital herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Oral Herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Orchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tooth Abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Ear lobe infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	VX-765 900 mg - Part A	VX-765 1200 mg - Part A	VX-765 - Overall Part B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 11 (54.55%)	8 / 11 (72.73%)	35 / 43 (81.40%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Angiomyolipoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Drug Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0

Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	3 / 43 (6.98%)
occurrences (all)	1	0	4
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pneumonia Aspiration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Affect Lability			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Dysphemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Stress			

subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	4 / 43 (9.30%)
occurrences (all)	0	0	5
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Investigations			
Anticonvulsant Drug Level Increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Blood urine present			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	3 / 43 (6.98%)
occurrences (all)	2	1	9
Procedural Pain			

subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	1
Hand fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Cartilage injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Lip injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Muscle Strain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	8 / 43 (18.60%)
occurrences (all)	0	3	13
Burning Sensation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Cerebellar Atrophy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	1	0	2

Head Discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Hyporeflexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Sedation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Convulsion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	3 / 43 (6.98%)
occurrences (all)	0	0	3
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	2
Postictal paralysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Status epilepticus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1

Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Eye Irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vision Blurred			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Blepharospasm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	1	0	2
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	3 / 43 (6.98%)
occurrences (all)	0	0	3

Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 43 (2.33%)
occurrences (all)	0	1	2
Food poisoning			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	2	1	0
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	0 / 43 (0.00%)
occurrences (all)	0	3	0
Abdominal Pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Dry Mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Frequent Bowel Movements			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia Oral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0

Tongue Disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Hepatic Function Abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Increased Tendency to Bruise			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Pruritus Generalised			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1

Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	4 / 43 (9.30%)
occurrences (all)	0	1	5
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Acute Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Orchitis			

subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Tooth Abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Ear lobe infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	2 / 11 (18.18%)	3 / 43 (6.98%)
occurrences (all)	1	2	3
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2012	Added an interim analysis for the evaluation of efficacy endpoints to assist with the planning of clinical development activities with VX-765.
13 April 2012	Added "Part A" and "Part B". "Part A" included the randomized, double-blind, placebo-controlled, parallel-group, dose-ranging part of the study and "Part B" included the OLE.
23 April 2012	Clarified the Day 92 assessments in Part B.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Decimal point consistency could not be maintained as EudraCT system does not recognize the trailing zero after decimal point.

Notes: