



## Clinical trial results:

### A Phase 2, Single-Blind, Placebo-Controlled Study to Evaluate the Effect of VX-770 on Hyperpolarized Helium-3 Magnetic Resonance Imaging in Subjects With Cystic Fibrosis, the G551D Mutation, and FEV1 40% Predicted

#### Summary

EudraCT number	2017-000672-28
Trial protocol	Outside EU/EEA
Global end of trial date	12 February 2013

#### Results information

Result version number	v1 (current)
This version publication date	08 June 2017
First version publication date	08 June 2017

#### Trial information

##### Trial identification

Sponsor protocol code	VX10-770-107
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01161537
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 6173416777, medical_info@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 6173416777, medical_info@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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 June 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 February 2013
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of VX-770 on hyperpolarized helium-3 magnetic resonance imaging (3He-MRI) in subjects aged 12 years and older with CF who have the G551D-CFTR mutation on at least 1 allele

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	13
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	9
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Study was initiated on October 10, 2010 after first eligible subject signed informed consent form and enrolled in study.

### Pre-assignment

Screening details:

All results were planned to be reported separately for Part A and Part B of the study.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

### Arms

Are arms mutually exclusive?	No
Arm title	Part A: VX-770

Arm description:

Subjects received placebo tablets matched to VX-770 150 mg orally twice daily from Day 1 to 14 (Placebo run-in period), followed by VX-770 150 mg tablets orally twice daily from Day 15 to 42 (VX-770 treatment period), and then placebo tablets matched to VX-770 150 mg orally twice daily from Day 43 to 57 (Placebo washout period) during Part A of the study.

Arm type	Experimental
Investigational medicinal product name	VX-770
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-770 150 mg film coated tablets orally twice daily from Day 15 to 42 (VX-770 treatment period).

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

Dosage and administration details:

Placebo tablets matched to VX-770 150 milligram (mg) orally twice daily from Day 1 to 14 (Placebo run-in period) and from Day 43 to 57 (Placebo washout period).

Arm title	Part B: VX-770
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Arm description:

Subjects received VX-770 150 mg tablets orally twice daily for 48 weeks during Part B of the study. Part B included subjects from Part A and newly enrolled subjects.

Arm type	Experimental
Investigational medicinal product name	VX-770
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

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**Dosage and administration details:**

Subjects received VX-770 150 mg film coated tablets orally twice daily for 48 weeks.

<b>Number of subjects in period 1</b>	Part A: VX-770	Part B: VX-770
Started	8	9
Completed	8	7
Not completed	0	2
Consent withdrawn by subject	-	2

## Baseline characteristics

### Reporting groups

Reporting group title	Part A: VX-770
Reporting group description:	
Subjects received placebo tablets matched to VX-770 150 mg orally twice daily from Day 1 to 14 (Placebo run-in period), followed by VX-770 150 mg tablets orally twice daily from Day 15 to 42 (VX-770 treatment period), and then placebo tablets matched to VX-770 150 mg orally twice daily from Day 43 to 57 (Placebo washout period) during Part A of the study.	
Reporting group title	Part B: VX-770
Reporting group description:	
Subjects received VX-770 150 mg tablets orally twice daily for 48 weeks during Part B of the study. Part B included subjects from Part A and newly enrolled subjects.	

Reporting group values	Part A: VX-770	Part B: VX-770	Total
Number of subjects	8	9	17
Age categorical			
Units: Subjects			
Age continuous			
Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: years			
arithmetic mean	18.9	24.4	
standard deviation	± 4.64	± 10.3	-
Gender categorical			
Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Subjects			
Female	4	3	7
Male	4	6	10
Race			
Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Subjects			
Race: White	7	9	16
Race: Black or African American	1	0	1
Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)			
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Predicted FEV1 (for age, gender, and height) was calculated using the Knudson method. Number of subjects in each percent predicted FEV1 category (less than [ $<$ ] 70%, greater than or equal to [ $\geq$ ] 70%–<90%, and $\geq$ 90%) are reported. Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Subjects			
<70%	2	6	8
$\geq$ 70%–<90%	1	1	2
$\geq$ 90%	5	2	7
Ethnicity			

Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Subjects			
Not Hispanic or Latino	8	9	17
Body Weight			
Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Kilogram (Kg)			
arithmetic mean	66.31	66.53	
standard deviation	± 14.393	± 13.693	-
Height			
Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Centimeter (cm)			
arithmetic mean	167.5	169.9	
standard deviation	± 9.66	± 11.82	-
Body Mass Index (BMI)			
BMI = (Weight [in kg]) divided by (Height [in meters]) <sup>2</sup> . Data was planned to be reported separately for Part A and Part B of the study. Some of the subjects were counted in more than one reporting arm.			
Units: Kilogram per square meter (kg/m <sup>2</sup> )			
arithmetic mean	23.44	22.96	
standard deviation	± 3.57	± 4.066	-

## End points

### End points reporting groups

Reporting group title	Part A: VX-770
Reporting group description: Subjects received placebo tablets matched to VX-770 150 mg orally twice daily from Day 1 to 14 (Placebo run-in period), followed by VX-770 150 mg tablets orally twice daily from Day 15 to 42 (VX-770 treatment period), and then placebo tablets matched to VX-770 150 mg orally twice daily from Day 43 to 57 (Placebo washout period) during Part A of the study.	
Reporting group title	Part B: VX-770
Reporting group description: Subjects received VX-770 150 mg tablets orally twice daily for 48 weeks during Part B of the study. Part B included subjects from Part A and newly enrolled subjects.	
Subject analysis set title	Part A : Placebo Run in/Washout
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects who received placebo tablets matched to VX-770 150 mg orally twice daily from Day 1 to 14 (Placebo run-in period) and from Day 43 to 57 (Placebo washout period) during Part A of the study were assessed between Day 1 to 14 and Day 43 to 57 of Part A.	

### Primary: Part A: Change From Baseline in Total Ventilation Defect Defined by Hyperpolarized Helium 3 Magnetic Resonance Imaging (3He-MRI) at Day 43

End point title	Part A: Change From Baseline in Total Ventilation Defect Defined by Hyperpolarized Helium 3 Magnetic Resonance Imaging (3He-MRI) at Day 43 <sup>[1][2]</sup>
End point description: Subjects inhaled hyperpolarized helium-3 (3He) gas mixed with nitrogen to make a total volume of approximately one-third forced vital capacity (FVC) to a maximum of 1 liter and hold their breath for 20 seconds or less. Rapid magnetic resonance imaging (MRI) was performed during inhalation/exhalation and/or breath-hold. Areas of decreased ventilation were observed as ventilation defects that are visualized as decreased (and/or absent) 3He intensity in 3He-MRI. The total ventilation defect was defined as the ratio of total ventilation defect volume (L) to total lung volume (L), expressed as a percentage. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in VX-770 treatment phase (Day 15 to 42). Full Analysis Set (FAS) included all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part A.	
End point type	Primary
End point timeframe: Part A: Baseline (pre-dose Day 15), Day 43	

#### 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: Only descriptive statistics were reported, inferential statistics were not planned for this primary endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms which are applicable to the endpoint are reported.

<b>End point values</b>	Part A: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of total lung volume				
arithmetic mean (standard deviation)	-8.2 (± 9.013)			

## Statistical analyses

No statistical analyses for this end point

### Primary: Part B: Change From Baseline in Total Ventilation Defect Defined by Hyperpolarized Helium 3 Magnetic Resonance Imaging (3He-MRI) at Week 48

End point title	Part B: Change From Baseline in Total Ventilation Defect Defined by Hyperpolarized Helium 3 Magnetic Resonance Imaging (3He-MRI) at Week 48 <sup>[3]</sup> <sup>[4]</sup>
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#### End point description:

Subjects were asked to inhale hyperpolarized 3 He gas mixed with nitrogen to make a total volume of approximately one-third forced vital capacity (FVC) to a maximum of 1 liter and hold their breath for 20 seconds or less. Rapid MRI was performed during inhalation/exhalation and/or breath-hold. Areas of decreased ventilation were observed as ventilation defects that are visualized as decreased (and/or absent) 3He intensity in 3He MRI. The total ventilation defect was defined as the ratio of total ventilation defect volume (L) to total lung volume (L), expressed as a percentage. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in Part B (48 weeks). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770) in Part B.

End point type	Primary
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#### End point timeframe:

Part B: Baseline (Day -1), Week 48

#### 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: Only descriptive statistics were reported, inferential statistics were not planned for this primary endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms which are applicable to the endpoint are reported.

End point values	Part B: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percentage of total lung volume				
arithmetic mean (standard deviation)	-6.33 (± 11.859)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Related AEs

End point title	Part A: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Related AEs <sup>[5]</sup>
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#### End point description:

AE: Any adverse change from subject's baseline condition, including any adverse experience, abnormal recording/clinical laboratory assessment which occurs during course of study, whether it is considered related to study drug or not. SAE: medical event or condition, which falls into any of following categories, regardless of its relationship to study drug: death, life threatening adverse experience, in-patient hospitalization/prolonged hospitalization, persistent/significant disability/incapacity, congenital anomaly/birth defect, important medical event. Related AEs includes all AEs for which causality was either related to study drug or possibly related to study drug. Safety analysis set includes all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part A. Data was reported as per intervention received (Placebo [Placebo Run in/Washout] or VX-770 [VX-770 Treatment]).



End point type	Secondary			
End point timeframe:				
Part A: Day 1 up to Day 57				
Notes:				
[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.				
End point values	Part A: VX-770	Part A : Placebo Run in/Washout		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	8	8		
Units: Subjects				
number (not applicable)				
AEs	3	2		
SAEs	0	0		
Related AEs	0	0		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) at Day 43

End point title	Part A: Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) at Day 43 <sup>[6]</sup>			
End point description:				
FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Predicted FEV1 (for age, gender, and height) was calculated using the Knudson method. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in VX-770 treatment phase (Day 15 to 42). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part A.				
End point type	Secondary			
End point timeframe:				
Part A: Baseline (pre-dose Day 15), Day 43				
Notes:				
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.				
End point values	Part A: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percent predicted of FEV1				
arithmetic mean (standard deviation)	12.78 (± 9.203)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Absolute Change From Baseline in Sweat Chloride at Day 43

End point title	Part A: Absolute Change From Baseline in Sweat Chloride at Day 43 <sup>[7]</sup>
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End point description:

Sweat samples were collected using an approved Macroduct (Wescor, Logan, Utah) collection device. A volume of greater than or equal to ( $\geq$ ) 15 microliter was required for determination of sweat chloride. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in VX-770 treatment phase (Day 15 to 42). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part A.

End point type	Secondary
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End point timeframe:

Part A: Baseline (pre-dose Day 15), Day 43

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.

<b>End point values</b>	Part A: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Millimole per liter (mmol/L)				
arithmetic mean (standard deviation)	-42.31 ( $\pm$ 13.475)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Absolute Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score At Day 43

End point title	Part A: Absolute Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score At Day 43 <sup>[8]</sup>
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End point description:

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in VX-770 treatment phase (Day 15 to 42). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part A.

End point type	Secondary
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End point timeframe:

Baseline (pre-dose Day 15), Day 43

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.

<b>End point values</b>	Part A: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Units on a scale				
arithmetic mean (standard deviation)	-7.64 (± 27.529)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Related AEs

End point title	Part B: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Related AEs <sup>[9]</sup>
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End point description:

AE: any adverse change from subject's baseline (pre-treatment) condition, including any adverse experience, abnormal recording/clinical laboratory assessment which occurs during course of study, whether it is considered related to study drug or not. SAE: medical event or condition, which falls into any of following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, in-patient hospitalization/prolonged hospitalization, persistent/significant disability/incapacity, congenital anomaly/birth defect, important medical event. Related AEs includes all AEs for which the causality was either related to study drug or possibly related to study drug. Safety analysis set included all enrolled subjects who received at least 1 dose of study drug (VX-770 or placebo) in Part B.

End point type	Secondary
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End point timeframe:

Part B: Day 1 up to Week 48

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only arms which are applicable to the endpoint are reported.

<b>End point values</b>	Part B: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Subjects				
AEs	6			
SAEs	1			
Related AEs	4			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) at Week 48

End point title	Part B: Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) at Week 48 <sup>[10]</sup>
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End point description:

FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Predicted FEV1 (for age, gender, and height) was calculated using the Knudson method. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in Part B (48 weeks). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770) in Part B. Here, "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Part B: Baseline (Day -1), Week 48

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms which are applicable to the endpoint are reported.

End point values	Part B: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percent predicted of FEV1				
arithmetic mean (standard deviation)	5.17 (± 9.422)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Absolute Change From Baseline in Sweat Chloride at Week 48

End point title	Part B: Absolute Change From Baseline in Sweat Chloride at Week 48 <sup>[11]</sup>
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End point description:

Sweat samples were collected using an approved Macroduct (Wescor, Logan, Utah) collection device. A volume of greater than or equal to ( $\geq$ ) 15 microliter was required for determination of sweat chloride. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in Part B (48 weeks). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770) in Part B. Here, "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Part B: Baseline (Day -1), Week 48

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms which are applicable to the endpoint are reported.

End point values	Part B: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: mmol/L				
arithmetic mean (standard deviation)	-48.88 (± 22.271)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Absolute Change From Baseline in in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score At Week 48

End point title	Part B: Absolute Change From Baseline in in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Respiratory Domain Score At Week 48 <sup>[12]</sup>
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#### End point description:

The CFQ-R is a validated patient-reported outcome measuring health-related quality of life for subjects with cystic fibrosis. Respiratory domain assessed respiratory symptoms (for example, coughing, congestion, wheezing), score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. Baseline was defined as the most recent non-missing measurement collected before initial administration of study drug in Part B (48 weeks). FAS included all enrolled subjects who received at least 1 dose of study drug (VX-770) in Part B. Here, "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary
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#### End point timeframe:

Part B: Baseline (Day -1), Week 48

#### Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms which are applicable to the endpoint are reported.

<b>End point values</b>	Part B: VX-770			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Units on a scale				
arithmetic mean (standard deviation)	15.08 (± 7.667)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Part A: Day 1 through Day 57; Part B: Day 1 through Week 48

Adverse event reporting additional description:

Subject with multiple events within a system organ class or preferred term was counted only once within the system organ class or preferred term, respectively.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

### Reporting groups

Reporting group title	Part A: Placebo Run in/Washout
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Reporting group description:

Subjects who received placebo tablets matched to VX-770 150 mg orally twice daily from Day 1 to 14 (Placebo run-in period) and from Day 43 to 57 (Placebo washout period) during Part A of the study were assessed between Day 1 to 14 and Day 43 to 57 of Part A.

Reporting group title	Part A: VX-770 Treatment
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Reporting group description:

Subjects who received VX-770 150 mg tablets orally twice daily from Day 15 to 42 (VX-770 treatment period), during Part A of the study were assessed between Day 15 to 42 of Part A.

Reporting group title	Part B: VX-770 Treatment
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Reporting group description:

Subjects who received VX-770 150 mg tablets orally twice daily for 48 weeks during Part B of the study were assessed between Day 1 to Week 48 of Part B. Part B included subjects from Part A and newly enrolled subjects.

Serious adverse events	Part A: Placebo Run in/Washout	Part A: VX-770 Treatment	Part B: VX-770 Treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	
Infections and infestations			
INFECTIVE PULMONARY EXACERBATION OF CYSTIC FIBROSIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
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: 5 %

<b>Non-serious adverse events</b>	Part A: Placebo Run in/Washout	Part A: VX-770 Treatment	Part B: VX-770 Treatment
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 8 (25.00%)	3 / 8 (37.50%)	6 / 9 (66.67%)
Investigations			
BODY MASS INDEX INCREASED subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
SPIROMETRY ABNORMAL subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
BACTERIAL TEST POSITIVE subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
STRESS FRACTURE subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
CYSTIC FIBROSIS LUNG subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
HEADACHE subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
PAIN subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
PYREXIA subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	3
Ear and labyrinth disorders			
CERUMEN IMPACTION alternative dictionary used: MedDRA 12.0			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Gastrointestinal disorders ABDOMINAL DISTENSION subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 8 (12.50%) 1	0 / 9 (0.00%) 0
ABDOMINAL PAIN alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
NAUSEA subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Respiratory, thoracic and mediastinal disorders DRY THROAT subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 0	0 / 9 (0.00%) 0
COUGH subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 2
Musculoskeletal and connective tissue disorders TENDONITIS subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	1 / 9 (11.11%) 1
Infections and infestations UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 8 (0.00%) 0	4 / 9 (44.44%) 4
INFECTIVE PULMONARY			



EXACERBATION OF CYSTIC FIBROSIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
BRONCHITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CELLULITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
LABYRINTHITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
NASOPHARYNGITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2010	- The Removal of Subjects section and the section for Elevation of Liver Function Test Parameters were revised.
10 January 2011	- Interim analysis of data added.
04 March 2011	- Limit on FEV1 severity categories removed from the protocol to allow evaluation of additional subjects.
16 May 2011	- Identified the original components of the study as "Part A" to distinguish these from the new, open-label, 48-week part of the study identified as "Part B", which was added to evaluate the long-term effect of VX-770 on 3 He-MRI.
03 August 2011	- Age limit for part B of the study was changed.
20 March 2012	- Screening ophthalmologic examination was added to Part B.
01 November 2012	- Total study duration was shortened; - Commercially available VX-770 (Kalydeco™) was added to the list of prohibited medications.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported