



Clinical trial results:

A Phase 2, Open-label Extension Study to Investigate the Long term Safety and Tolerability of PF-06649751 in Subjects with Motor Fluctuations due to Parkinson's Disease

Summary

EudraCT number	2017-000128-81
Trial protocol	DE ES
Global end of trial date	25 October 2017

Results information

Result version number	v1 (current)
This version publication date	13 March 2019
First version publication date	13 March 2019

Trial information

Trial identification

Sponsor protocol code	B7601017
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03185481
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc, +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2017
Global end of trial reached?	Yes
Global end of trial date	25 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the long term safety and tolerability of PF-06649751 administered once daily (QD) in subjects with Parkinson's disease.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2017
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: 5
Worldwide total number of subjects	5
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)	0
Adults (18-64 years)	2
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Five (5) subjects were assigned to treatment and treated.

Period 1

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

Blinding implementation details:

The study was single-blinded 4 subjects who were delayed rollover subjects, and double-blinded for 1 subject who was direct rollover subject.

Arms

Arm title	PF-06649751 15 mg
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Arm description:

Participants who completed Week 15 in Study B7601003 (NCT02687542) were orally administered PF-06649751 once daily (QD) at the last dose level used in Study B7601003 (1 mg, 3 mg, 7 mg or 15 mg, and original placebo participants starting from 1 mg) titrated up to 15 mg during a 3-week titration period, followed by a 2-week dose adjustment period (15 mg or if intolerance, reduced to 7 mg) and then followed by open-label maintenance treatment of PF-06649751 15 mg QD for 44 weeks or until discontinuation.

Arm type	Experimental
Investigational medicinal product name	PF-06649751
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PF-06649751 were orally administered once daily (QD) at the last dose level used in Study B7601003 (1 mg, 3 mg, 7 mg or 15 mg, and original placebo participants starting from 1 mg) titrated up to 15 mg during a 3-week titration period, followed by a 2-week dose adjustment period (15 mg or if intolerance, reduced to 7 mg) and then followed by open-label maintenance treatment of PF-06649751 15 mg QD for 44 weeks or until discontinuation.

Number of subjects in period 1	PF-06649751 15 mg
Started	5
Completed	0
Not completed	5
Adverse event, non-fatal	1
Study Terminated by Sponsor	4

Baseline characteristics

Reporting groups

Reporting group title	PF-06649751 15 mg
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Reporting group description:

Participants who completed Week 15 in Study B7601003 (NCT02687542) were orally administered PF-06649751 once daily (QD) at the last dose level used in Study B7601003 (1 mg, 3 mg, 7 mg or 15 mg, and original placebo participants starting from 1 mg) titrated up to 15 mg during a 3-week titration period, followed by a 2-week dose adjustment period (15 mg or if intolerance, reduced to 7 mg) and then followed by open-label maintenance treatment of PF-06649751 15 mg QD for 44 weeks or until discontinuation.

Reporting group values	PF-06649751 15 mg	Total	
Number of subjects	5	5	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	3	3	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	63		
standard deviation	± 11.73	-	
Sex: Female, Male			
Units: Subjects			
Female	0	0	
Male	5	5	
Race/Ethnicity, Customized			
Units: Subjects			
White	5	5	
Black or African American	0	0	
Asian	0	0	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Other	0	0	
Unknown	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	5	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	PF-06649751 15 mg
Reporting group description: Participants who completed Week 15 in Study B7601003 (NCT02687542) were orally administered PF-06649751 once daily (QD) at the last dose level used in Study B7601003 (1 mg, 3 mg, 7 mg or 15 mg, and original placebo participants starting from 1 mg) titrated up to 15 mg during a 3-week titration period, followed by a 2-week dose adjustment period (15 mg or if intolerance, reduced to 7 mg) and then followed by open-label maintenance treatment of PF-06649751 15 mg QD for 44 weeks or until discontinuation.	

Primary: Number of Subjects with Treatment-Emergent Adverse Events (All Causalities)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (All Causalities) ^[1]
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End point description:

An adverse event (AE) is any untoward medical occurrence in a study subject administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. Any AE occurring following the start of treatment or occurring before treatment but increasing in severity afterward were counted as treatment-emergent AE (TEAE).

End point type	Primary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Treatment-Emergent Adverse Events (Treatment Related)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (Treatment Related) ^[2]
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End point description:

An adverse event (AE) is any untoward medical occurrence in a study subject administered a product or medical device. Any AE occurring following the start of treatment or occurring before treatment but increasing in severity afterward were counted as treatment-emergent AE (TEAE).

End point type	Primary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

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 this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Clinically Significant Findings in Physical Examination

End point title	Number of Subjects with Clinically Significant Findings in Physical Examination ^[3]
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End point description:

A full physical examination included head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal and musculoskeletal systems. The brief physical examination was focused on general appearance, pulmonary, abdominal exams, the respiratory and cardiovascular systems, as well as towards subjects reported symptoms. The clinical significance was determined by the investigator.

End point type	Primary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Clinically Significant Findings in Neurological Examination

End point title	Number of Subjects with Clinically Significant Findings in Neurological Examination ^[4]
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End point description:

The full neurological examination included assessment of the visual fields and of the right and left optic fundus; cranial nerves; mental state; muscle strength and tone, abnormal movements; deep tendon reflexes; sensory exam, coordination, gait and station. Higher cortical and motor function was

considered part of the complete neurological exam. The brief neurological exam included observation for cerebellar (intention) tremor and for non cerebellar tremors (eg, resting or positional), finger to nose, heel to shin, Romberg, gait and tandem walking, positional and gaze evoked nystagmus. The clinical significance was determined by the investigator.

End point type	Primary
End point timeframe:	
Baseline to last visit after termination (up to approximately 3 months)	

Notes:

[4] - 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 this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Abnormalities in Laboratory Test (Without Regard to Baseline Abnormality)

End point title	Number of Subjects with Abnormalities in Laboratory Test (Without Regard to Baseline Abnormality) ^[5]
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End point description:

Laboratory tests included hematology(hemoglobin,hematocrit,red and white blood cell count,mean corpuscular volume,mean corpuscular hemoglobin,mean corpuscular hemoglobin concentration,platelet count,neutrophils,eosinophils,monocytes, basophils,lymphocytes), chemistry(blood urea nitrogen/urea and creatinine,fasting glucose, calcium,sodium,potassium, chloride,total carbon dioxide,aspartate and alanine aminotransferase,total bilirubin,alkaline phosphatase,uric acid,albumin,total protein),urinalysis(pH,qualitative glucose protein,blood,ketones,nitrites,leukocyte esterase,urobilinogen,urine bilirubin,microscopy,specific gravity,urine creatinine),other tests(urine drug screen,follicle stimulating hormone,anti neutrophil cytoplasmic antibody panel,qualitative antinuclear antibody,fibrinogen,C reactive protein,erythrocyte sedimentation rate,C3, C4, CH50/CH100,rheumatoid factor,immunoglobulin panel,if anti- neutrophil cytoplasmic antibody positive:proteinase 3

End point type	Primary
End point timeframe:	
Baseline to last visit after termination(up to approximately 3 months)	

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Vital Signs Data Meeting Pre-defined Criteria

End point title	Number of Subjects with Vital Signs Data Meeting Pre-defined Criteria ^[6]
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End point description:

Number of subjects with vital signs findings meeting the following criteria is presented: (1) standing diastolic blood pressure (DBP) increase from baseline $\geq$ 20 mm Hg; (2) standing SBP increase from baseline $\geq$ 30 mm Hg; (3) supine DBP increase from baseline $\geq$ 20 mm Hg; (4) supine systolic blood pressure (SBP) increase from baseline $\geq$ 30 mm Hg; (5) standing DBP decrease from baseline $\geq$ 20 mm Hg; (6) standing SBP decrease from baseline $\geq$ 30 mm Hg; (7) supine DBP decrease from baseline $\geq$ 20 mm Hg; (8) supine SBP decrease from baseline $\geq$ 30 mm Hg.

End point type	Primary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

Notes:

[6] - 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 this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects				
Standing DBP increase from baseline $\geq$ 20 mm Hg	0			
Standing SBP increase from baseline $\geq$ 30 mm Hg	1			
Supine DBP increase from baseline $\geq$ 20 mm Hg	0			
Supine SBP increase from baseline $\geq$ 30 mm Hg	2			
Standing DBP decrease from baseline $\geq$ 20 mm Hg	0			
Standing SBP decrease from baseline $\geq$ 30 mm Hg	0			
Supine DBP decrease from baseline $\geq$ 20 mm Hg	0			
Supine SBP decrease from baseline $\geq$ 30 mm Hg	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Vital Signs Data of Orthostatic Hypotension Meeting Pre-defined Criteria

End point title	Number of Subjects with Vital Signs Data of Orthostatic Hypotension Meeting Pre-defined Criteria ^[7]
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End point description:

Orthostatic hypotension was defined as a decrease of $\geq$ 20 mmHg for systolic blood pressure (SBP) or $\geq$ 10 mmHg for diastolic blood pressure (DBP) 2 minutes after standing from a supine position.

End point type	Primary
End point timeframe:	
Baseline to last visit after termination (up to approximately 3 months)	
Notes:	
[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: No statistical analysis was planned for this endpoint	

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects				
DBP postural difference ≥ 10 mmHg (Supine-Standing)	3			
SBP postural difference ≥ 20 mmHg (Supine-Standing)	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Electrocardiogram Data Meeting Pre-defined Criteria

End point title	Number of Subjects with Electrocardiogram Data Meeting Pre-defined Criteria ^[8]
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End point description:

PR interval (time from the beginning of P wave to the start of QRS complex, corresponding to the end of atrial depolarization and onset of ventricular depolarization), QRS duration (time from Q wave to the end of S wave, corresponding to ventricle depolarization), QT interval (time from the beginning of Q wave to the end of T wave) and QTcF interval (QT interval corresponding to electrical systole corrected for heart rate using Fridericia's formula) are summarized. Number of subjects with ECG findings meeting the following criteria is presented: (1) PR interval ≥ 300 msec; (2) QRS duration ≥ 140 msec; (3) QT interval ≥ 500 ; (4) QTcF interval: 450 to <480 msec; (5) QTcF interval: 480 to <500 msec; (6) QTcF interval ≥ 500 msec.

End point type	Primary
End point timeframe:	
Baseline to last visit after termination (up to approximately 3 months)	

Notes:

[8] - 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 this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects				
PR Interval (aggregate) ≥ 300 msec	0			
QRS Duration (aggregate) ≥ 140 msec	0			
QT Interval (aggregate) ≥ 500 msec	0			
QTcF Interval (aggregate) ≥ 450 msec, <480 msec	0			

QTcF Interval (aggregate) >= 480 msec, <500msec	0			
QTcF Interval (aggregate) >= 500 msec	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Worsening Suicidality and New Onset Suicidality

End point title	Number of Subjects with Worsening Suicidality and New Onset Suicidality ^[9]
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End point description:

The Columbia Suicide Severity Rating Scale (C-SSRS) is an interview based rating scale to systematically assess suicidal ideation and suicidal behavior. At each suicidality assessment, subjects felt to have significant suicidal ideation with actual plan and intent or suicidal behavior, must be evaluated by a clinician/mental health professional (MHP) skilled in the evaluation of suicidality in the subjects by virtue of training or experience who determined if it is safe for the subjects to participate/continue in the trial. The denominator used in the percentages was the number of subjects assessed for suicidality or worsening, the denominator included the subset of subjects who had any level of suicidality reported at baseline. For new onset, the denominator included the subset of subjects with no suicidality reported at baseline.

End point type	Primary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Subjects				
New Onset	0			
Worsening	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Benzodiazepine Discontinuation Symptoms Based on Physician Withdrawal Checklist (PWC-20)

End point title	Number of Subjects With Benzodiazepine Discontinuation Symptoms Based on Physician Withdrawal Checklist (PWC-20) ^[10]
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End point description:

The PWC-20 is a physician-completed, 20-item reliable and sensitive instrument for the assessment of benzodiazepine discontinuation symptoms, including anxiety and nervous, depersonalization and derealization, diarrhea, diaphoresis, difficulty concentrating and remembering, dizziness-lightheadedness, depression, fatigue, lethargy and lack of energy, headaches, increased acuity for sound, smell, touch, or pain, insomnia, irritability, loss of appetite, muscle aches or stiffness, nausea-

vomiting paresthesias, poor coordination, restlessness and agitation, tremor-tremulousness, and weakness. Summaries of the count of subjects experiencing symptoms and severity listed in the PWC-20 were provided.

End point type	Primary
End point timeframe:	
At last visit	

Notes:

[10] - 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 this endpoint

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Subjects				
Anxiety, Nervousness: Not Present	3			
Difficult Concentrating, Remembering: Not Present	3			
Dysphoric Mood, Depression: Not Present	3			
Fatigue, Lethargy, Lack of Energy: Not Present	2			
Insomnia: Not Present	2			
Irritability: Not Present	3			
Muscle Aches or Stiffness: Not Present	3			
Poor Coordination: Not Present	2			
Restlessness, Agitation: Not Present	3			
Tremor-Tremulousness: Not Present	3			
Weakness: Not Present	2			
Anxiety, Nervousness: Mild	1			
Difficult Concentrating, Remembering: Mild	1			
Dysphoric Mood, Depression: Mild	1			
Fatigue, Lethargy, Lack of Energy: Mild	1			
Insomnia: Mild	1			
Irritability: Mild	0			
Muscle Aches or Stiffness: Mild	0			
Poor Coordination: Mild	1			
Restlessness, Agitation: Mild	0			
Tremor-Tremulousness: Mild	0			
Weakness: Mild	2			
Anxiety, Nervousness: Moderate	0			
Difficult Concentrating, Remembering: Moderate	0			
Dysphoric Mood, Depression: Moderate	0			
Fatigue, Lethargy, Lack of Energy: Moderate	1			
Insomnia: Moderate	1			
Irritability: Moderate	1			
Muscle Aches or Stiffness: Moderate	1			
Poor Coordination: Moderate	1			
Restlessness, Agitation: Moderate	1			
Tremor-Tremulousness: Moderate	0			
Weakness: Moderate	0			

Anxiety, Nervousness: Severe	0			
Difficult Concentrating, Remembering: Severe	0			
Dysphoric Mood, Depression: Severe	0			
Fatigue, Lethargy, Lack of Energy: Severe	0			
Insomnia: Severe	0			
Irritability: Severe	0			
Muscle Aches or Stiffness: Severe	0			
Poor Coordination: Severe	0			
Restlessness, Agitation: Severe	0			
Tremor-Tremulousness: Severe	1			
Weakness: Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline for Hauser Subject Diary Data in Daily OFF Time

End point title	Change from Baseline for Hauser Subject Diary Data in Daily OFF Time
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End point description:

Available diaries are designed to record subjects motor state for half hour intervals. These diaries are a way for subjects to assess their own health status without clinician bias or interpretation. In subjects diaries, "OFF" time is defined as a period when medication has worn off and is no longer providing benefit with regard to mobility, slowness, and stiffness. During this period, Parkinson's Disease (PD) subjects experience relatively poor overall function with worsening of tremor, rigidity, balance, or bradykinesia.

End point type	Secondary
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End point timeframe:

Baseline, Day 21 and Day 35

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Hours				
arithmetic mean (standard deviation)				
Baseline	3.25 ($\pm$ 0)			
Day 21	0.00 ($\pm$ 0)			
Day 35	-0.42 ($\pm$ 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline for Hauser Subject Diary Data in Daily ON Time with Troublesome Dyskinesia

End point title	Change from Baseline for Hauser Subject Diary Data in Daily ON Time with Troublesome Dyskinesia
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End point description:

Available diaries are designed to record subjects motor state for half hour intervals. These diaries are a way for subjects to assess their own health status without clinician bias or interpretation. "ON" time is defined as the time when medication is providing benefit with regard to mobility, slowness, and stiffness. "ON" time can be classified as associated with or without troublesome dyskinesia that interfere with activities of daily living. It has been demonstrated that "ON" time with troublesome dyskinesia are generally considered by subjects to be "bad time" with regard to motor function.

End point type	Secondary
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End point timeframe:

Baseline, Day 21 and Day 35

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Hours				
arithmetic mean (standard deviation)				
Baseline	0.00 ($\pm$ 0)			
Day 21	0.00 ($\pm$ 0)			
Day 35	0.00 ($\pm$ 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline for Hauser Subject Diary Data in Daily ON Time Without Troublesome Dyskinesia

End point title	Change from Baseline for Hauser Subject Diary Data in Daily ON Time Without Troublesome Dyskinesia
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End point description:

Available diaries are designed to record subjects motor state for half hour intervals. These diaries are a way for subjects to assess their own health status without clinician bias or interpretation. "ON" time is defined as the time when medication is providing benefit with regard to mobility, slowness, and stiffness. "ON" time can be classified as associated with or without troublesome dyskinesia that interfere with activities of daily living. "ON" time without dyskinesia and on time with non troublesome dyskinesia are generally considered to be "good time".

End point type	Secondary
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End point timeframe:

Baseline, Day 21 and Day 35

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Hours				
arithmetic mean (standard deviation)				
Baseline	9.58 (± 0)			
Day 21	1.17 (± 0)			
Day 35	2.42 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I, II, III, IV, and Total Score

End point title	Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I, II, III, IV, and Total Score
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End point description:

The total MDS-UPDRS score developed by the Movement Disorder Society is the most common method of evaluating the severity of Parkinson's Disease (PD) across behaviors, activities of daily living, motor abilities, and other complications of PD. Part I assesses non motor experiences of daily living and is comprised of two components assessed by investigator and subjects respectively. Part II assesses motor experiences of daily living. There are an additional 13 questions that are also part of the Subject Questionnaire completed by the subjects. Part III assesses the motor signs of PD and is administered by the investigator. Part IV assesses motor complications, dyskinesias, and motor fluctuations using historical and objective information.

End point type	Secondary
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End point timeframe:

Baseline to last visit after termination (up to approximately 3 months)

End point values	PF-06649751 15 mg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Units on a scale				
median (full range (min-max))				
Part I Score	-1.5 (-15 to 9)			
Part II Score	0 (-10 to 9)			
Part III Score	-2.5 (-9 to 11)			
Part IV Score	0 (-3 to 6)			
Total Score	0 (-32 to 19)			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to last visit after termination (up to approximately 3 months)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	PF-06649751 15 mg
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Reporting group description:

Subjects who completed Week 15 in Study B7601003 (NCT02687542) were orally administered PF-06649751 once daily (QD) at the last dose level used in Study B7601003 (1 mg, 3 mg, 7 mg or 15 mg, and original placebo subjects starting from 1 mg) titrated up to 15 mg during a 3-week titration period, followed by a 2-week dose adjustment period (15 mg or if intolerance, reduced to 7 mg) and then followed by open-label maintenance treatment of PF-06649751 15 mg QD for 44 weeks or until discontinuation.

Serious adverse events	PF-06649751 15 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Hip Fracture			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	PF-06649751 15 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Vascular disorders			

Orthostatic hypotention subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2017	Updated Schedule of Activities and Section 1, 2, 3, 4, 5, 6, 7, 9 and 13; Added new Appendix 4; updated Appendix 3 reference

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.

This study was early terminated, not due to safety concern, but lack of sufficient demonstrated efficacy of the study drug to help improve PD symptoms in the parent study B7601003.
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Notes: