



Clinical trial results:

A 15-Week, Phase 2, Double Blind, Randomized, Placebo-Controlled, Dose Ranging Study to Investigate the Efficacy, Safety and Tolerability of PF-06649751 in Subjects With Motor Fluctuations Due to Parkinson's Disease

Summary

EudraCT number	2015-004912-39
Trial protocol	DE ES
Global end of trial date	10 November 2017

Results information

Result version number	v1 (current)
This version publication date	14 November 2018
First version publication date	14 November 2018

Trial information

Trial identification

Sponsor protocol code	B7601003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02687542
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 18007181021, 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	08 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2017
Global end of trial reached?	Yes
Global end of trial date	10 November 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the effect on motor symptoms of PF-06649751 administered once daily as adjunctive treatment with stable doses of L-Dopa in Parkinson's disease; and to determine the therapeutic window for motor symptom improvement of PF-06649751 administered once daily, ie, determining a dose, or a range of doses, for adequate control of motor symptoms.

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 Conference on 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 trial subjects.

Background therapy:

L-Dopa is one of the currently available pharmacological treatment strategies for Parkinson's disease. L-Dopa therapy provides increased dopamine levels in a transient and highly variable pulse and affords rapid onset improvement of motor symptoms for a limited duration. More than 40% of patients on L-Dopa experience motor fluctuations and dyskinesias after more than 3 to 5 years of therapy. Following an initial titration phase in this study, which was intended to mitigate potential dopaminergic adverse events such as nausea and vomiting, fixed doses of PF-06649751 were evaluated as adjunctive treatment with L-Dopa.

Subjects received Ldopa in accordance with instructions provided in the product labelling information, at a dose and frequency per the instructions of the investigator.

Evidence for comparator: -

Actual start date of recruitment	03 March 2016
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	Canada: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United States: 75
Worldwide total number of subjects	108
EEA total number of subjects	21

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)	50
From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 200 subjects were screened, of which 108 subjects were assigned to treatment: 23 subjects to placebo, 13 subjects to PF-06649751 1 mg once daily (QD), 15 subjects to 3 mg QD, 13 subjects to 7 mg QD and 44 subjects to 15 mg QD.

Period 1

Period 1 title	Overall Study (overall 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	Placebo

Arm description:

The subjects swallowed 3 tablets once daily (QD) at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks.

A follow-up visit was at Week 17, 2 weeks after discontinuation of Placebo. A follow-up phone visit was scheduled at Week 19 for subject's safety.

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:

3 Placebo tablets were taken once daily (QD) at approximately the same time each morning within approximately 5 minutes.

Arm title	PF-06649751 1 mg QD
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Arm description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa.

A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

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:

3 tablets containing 1 mg PF-06649751 were taken QD at approximately the same time each morning within approximately 5 minutes.

Arm title	PF-06649751 3 mg QD
Arm description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
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: 3 tablets containing 3 mg PF-06649751 were taken QD at approximately the same time each morning within approximately 5 minutes.	
Arm title	PF-06649751 7 mg QD

Arm description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
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: 3 tablets containing 7 mg PF-06649751 were taken QD at approximately the same time each morning within approximately 5 minutes.	
Arm title	PF-06649751 15 mg QD

Arm description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
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: 3 tablets containing 15 mg PF-06649751 were taken QD at approximately the same time each morning within approximately 5 minutes.	

Number of subjects in period 1	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD
Started	23	13	15
Completed	15	1	1
Not completed	8	12	14
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	3	1	3
Other	5	9	10
Medication error without associated AEs	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	PF-06649751 7 mg QD	PF-06649751 15 mg QD
Started	13	44
Completed	3	24
Not completed	10	20
Consent withdrawn by subject	2	4
Adverse event, non-fatal	2	9
Other	6	5
Medication error without associated AEs	-	1
Lost to follow-up	-	1
Protocol deviation	-	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

The subjects swallowed 3 tablets once daily (QD) at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks.

A follow-up visit was at Week 17, 2 weeks after discontinuation of Placebo. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 1 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa.

A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 3 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa.

A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 7 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa.

A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

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

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed.

Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa.

A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD
Number of subjects	23	13	15
Age categorical Units: Subjects			
Adults (< 65 years)	8	5	9
From 65-74 years	11	4	5

From 75-84 years	4	4	1
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Age Continuous Units: years arithmetic mean standard deviation	66.04 ± 8.79	66.92 ± 8.79	63.80 ± 7.76
Sex: Female, Male Units: Subjects			
Female	6	6	6
Male	17	7	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	0
White	20	12	12
Other	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	3	1
Not Hispanic or Latino	20	10	13
Unknown	0	0	1

Reporting group values	PF-06649751 7 mg QD	PF-06649751 15 mg QD	Total
Number of subjects	13	44	108
Age categorical Units: Subjects			
Adults (< 65 years)	3	25	50
From 65-74 years	7	14	41
From 75-84 years	3	5	17
Age Continuous Units: years arithmetic mean standard deviation	67.77 ± 9.36	63.41 ± 8.47	-
Sex: Female, Male Units: Subjects			
Female	4	18	40
Male	9	26	68
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	1	6	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	6
White	9	36	89
Other	0	1	2
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	1	3	11
Not Hispanic or Latino	12	40	95
Unknown	0	1	2

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: The subjects swallowed 3 tablets once daily (QD) at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks. A follow-up visit was at Week 17, 2 weeks after discontinuation of Placebo. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
Reporting group title	PF-06649751 1 mg QD
Reporting group description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
Reporting group title	PF-06649751 3 mg QD
Reporting group description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
Reporting group title	PF-06649751 7 mg QD
Reporting group description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	
Reporting group title	PF-06649751 15 mg QD
Reporting group description: The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.	

Primary: Change From Baseline in Daily OFF Time at Week 10

End point title	Change From Baseline in Daily OFF Time at Week 10
End point description: A paper Hauser diary was utilized to record motor state for half-hour intervals. Subjects completed the diary by answering whether they had been OFF for 3 consecutive days in the week prior to each visit (except Day 28 visit), including 3 consecutive days during the week prior to Day 0 (Randomization). The daily OFF time was calculated as the average of the 3 consecutive daily OFF hours from the Hauser	

diary at each visit.

Analysis population was Full Analysis Set consisting of all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary).

n in the following table represents the number of evaluable subjects in each arm.

End point type	Primary
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End point timeframe:

Week 10; Baseline was defined as the average daily OFF time (using 3 Hauser subject diary days) prior to Day -1 (study derived day and equalled to nominal visit day 0).

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Hours				
least squares mean (standard error)				
Change at Week 10 (n=16, 3, 2, 5 and 25)	-0.969 (\pm 0.4092)	-1.173 (\pm 0.3482)	-1.316 (\pm 0.3289)	-1.480 (\pm 0.3460)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hours				
least squares mean (standard error)				
Change at Week 10 (n=16, 3, 2, 5 and 25)	-1.663 (\pm 0.4297)			

Statistical analyses

Statistical analysis title	Bayesian Dose Response Analysis
Comparison groups	Placebo v PF-06649751 15 mg QD
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5776 ^[1]
Method	Bayesian Dose Response Analysis
Parameter estimate	Bayesian Dose Reponse Estimate
Point estimate	-0.693
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.713
upper limit	0.304
Variability estimate	Standard error of the mean
Dispersion value	0.6162

Notes:

[1] - Bayesian Predictive Test for Emax (the additive increase over Placebo in the response of PF-06649751 at a theoretically infinite dose) Monotonicity

Secondary: Change From Baseline in Daily OFF Time

End point title	Change From Baseline in Daily OFF Time
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End point description:

A paper Hauser diary was utilized to record motor state for half-hour intervals. Subjects completed the diary by answering whether they had been OFF for 3 consecutive days in the week prior to each visit (except Day 28 visit), including 3 consecutive days during the week prior to Day 0 (Randomization). The daily OFF time was calculated as the average of the 3 consecutive daily OFF hours from the Hauser diary at each visit.

Analysis population was Full Analysis Set consisting of all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary).

(n in the following table stands for number of subjects evaluable for each treatment arm).

Results at Week 15 should be interpreted with caution given almost half the subjects were not available for this analysis at Week 15 as compared to Week 10 and the complicated nature of protocol changes that impacted the study design after Week 10.

End point type	Secondary
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End point timeframe:

Weeks 3, 5, 10 and 15; Baseline was defined as the average daily OFF time (using 3 Hauser subject diary days) prior to Day -1 (study derived day and equalled to nominal visit day 0).

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Hours				
least squares mean (standard error)				
Change at Week 3 (n=18, 6, 8, 6 and 37)	-0.67 (± 0.620)	-0.82 (± 1.237)	-0.55 (± 1.091)	-1.82 (± 1.182)
Change at Week 5 (n=17, 5, 6, 7 and 32)	-0.63 (± 0.490)	-2.04 (± 1.054)	-2.23 (± 0.964)	-1.41 (± 0.937)
Change at Week 10 (n=16, 3, 2, 5 and 25)	-0.99 (± 0.628)	-0.60 (± 1.423)	-1.00 (± 1.508)	-2.07 (± 1.187)
Change at Week 15 (n=7, 1, 1, 3, and 14)	1.05 (± 1.063)	-0.67 (± 2.960)	-2.75 (± 2.936)	-1.09 (± 1.687)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hours				
least squares mean (standard error)				
Change at Week 3 (n=18, 6, 8, 6 and 37)	-1.01 (± 0.464)			
Change at Week 5 (n=17, 5, 6, 7 and 32)	-1.24 (± 0.392)			
Change at Week 10 (n=16, 3, 2, 5 and 25)	-1.63 (± 0.502)			
Change at Week 15 (n=7, 1, 1, 3, and 14)	-2.47 (± 0.793)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daily ON Time With Troublesome Dyskinesia

End point title	Change From Baseline in Daily ON Time With Troublesome Dyskinesia
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End point description:

A paper Hauser diary was utilized to record motor state for half-hour intervals. The subjects answered the Hauser diary on whether they had been ON with troublesome dyskinesia. A diary day started with the interval 24:00-0:30 through 23:30-24:00 on each chronological day for 3 consecutive days. On the days recording the home diary, subjects made an entry every 30 minutes during their normal waking time and upon awakening from time asleep. The daily ON hours was calculated as the average of the 3 consecutive daily ON hours from the Hauser diary at each visit. Full Analysis Set including all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary). (n in the following table stands for number of subjects evaluable for each treatment arm). Results at Week15 should be interpreted with caution given almost half subjects were not available for this analysis at Week15 compared to Week10 and complicated protocol changes impacting study design after Week10.

End point type	Secondary
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End point timeframe:

Weeks 3, 5, 10 and 15; Baseline was defined as the average daily ON time with Troublesome Dyskinesia (using 3 Hauser subject diary Days) prior to Day -1 (study derived day and equalled to nominal visit Day 0).

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Hours				
least squares mean (standard error)				
Change at Week 3 (n=18, 6, 8, 6 and 37)	0.17 (± 0.236)	0.07 (± 0.467)	0.19 (± 0.417)	0.01 (± 0.464)
Change at Week 5 (n=17, 5, 6, 7 and 32)	0.23 (± 0.198)	-0.21 (± 0.415)	-0.02 (± 0.388)	0.45 (± 0.363)
Change at Week 10 (n=16, 3, 2, 5 and 25)	0.13 (± 0.191)	0.24 (± 0.464)	0.32 (± 0.529)	-0.39 (± 0.389)
Change at Week 15 (n=7, 1, 1, 3 and 14)	0.01 (± 0.642)	-0.43 (± 1.349)	-0.29 (± 1.263)	0.54 (± 1.071)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hours				
least squares mean (standard error)				

Change at Week 3 (n=18, 6, 8, 6 and 37)	0.23 (\pm 0.179)			
Change at Week 5 (n=17, 5, 6, 7 and 32)	0.03 (\pm 0.162)			
Change at Week 10 (n=16, 3, 2, 5 and 25)	0.13 (\pm 0.167)			
Change at Week 15 (n=7, 1, 1, 3 and 14)	-0.21 (\pm 0.463)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daily ON Time Without Troublesome Dyskinesia

End point title	Change From Baseline in Daily ON Time Without Troublesome Dyskinesia
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End point description:

A paper Hauser diary was utilized to record motor state for half hour intervals. The subjects answered the Hauser diary on whether they had been ON without troublesome dyskinesia. A diary day started with the interval 24:00-0:30 through 23:30-24:00 on each chronological day for 3 consecutive days. On the days recording the home diary, subjects made an entry every 30 minutes during their normal waking time and upon awakening from time asleep. The daily ON hours was calculated as the average of the 3 consecutive daily ON hours from the Hauser diary at each visit. Full Analysis Set including all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary). (n in the following table is number of subjects evaluable for each treatment arm) Results at Week 15 should be interpreted with caution given almost half subjects were not available for this analysis at Week 15 compared to Week 10 and complicated protocol changes impacting study design after Week 10.

End point type	Secondary
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End point timeframe:

Weeks 3, 5, 10 and 15; Baseline was defined as the average daily ON time without Troublesome Dyskinesia (using 3 Hauser subject diary days) prior to Day -1 (study derived day and equalled to nominal visit Day 0).

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Hours				
least squares mean (standard error)				
Change at Week 3 (n=18, 6, 8, 6 and 37)	0.61 (\pm 0.577)	1.74 (\pm 1.173)	-0.49 (\pm 1.047)	1.93 (\pm 1.128)
Change at Week 5 (n=17, 5, 6, 7 and 32)	0.02 (\pm 0.548)	2.39 (\pm 1.150)	1.31 (\pm 1.058)	1.12 (\pm 1.029)
Change at Week 10 (n=16, 3, 2, 5 and 25)	0.61 (\pm 0.618)	0.92 (\pm 1.413)	0.45 (\pm 1.598)	2.64 (\pm 1.194)
Change at Week 15 (n=7, 1, 1, 3 and 14)	-0.81 (\pm 1.099)	0.37 (\pm 2.999)	-4.48 (\pm 3.192)	0.94 (\pm 1.781)

End point values	PF-06649751 15 mg QD			
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Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Hours				
least squares mean (standard error)				
Change at Week 3 (n=18, 6, 8, 6 and 37)	0.77 (\pm 0.443)			
Change at Week 5 (n=17, 5, 6, 7 and 32)	1.31 (\pm 0.436)			
Change at Week 10 (n=16, 3, 2, 5 and 25)	1.65 (\pm 0.508)			
Change at Week 15 (n=7, 1, 1, 3 and 14)	1.50 (\pm 0.825)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III

End point title	Change From Baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III
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End point description:

MDS-UPDRS Part III assessed the motor signs of Parkinson's disease and was administered by the investigator. It consisted of 33 sub-scores based on 18 items, several with right, left or other body distribution scores. Each question was anchored with 5 responses that are linked to commonly accepted clinical terms: 0=normal, 1=slight, 2=mild, 3=moderate, and 4=severe. Higher total scores indicated more severe motor signs of Parkinson's disease. There were 4 subscales: The tremor subscale (Score: 0-36); The rigidity subscale (Score: 0-20); The bradykinesia subscale (Score: 0-36); The Postural Instability and Gait Disorder subscale (Score: 0-12). Full Analysis Set consisting of all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary). (n is number of subjects evaluable for each treatment arm) Results at Week 15 should be interpreted with caution given almost half the subjects were not available for this analysis as compared to Week 10.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 3, 4, 5, 10 and 15; Baseline was defined as the Day -1 (study derived day and equalled to nominal visit Day 0) measurement

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Scale				
least squares mean (standard error)				
Change at Week 1 (n=21, 7, 9, 9 and 41)	-3.90 (\pm 2.054)	-4.44 (\pm 3.965)	-4.61 (\pm 3.593)	-1.90 (\pm 3.594)
Change at Week 2 (n=11, 1, 0, 1 and 20)	-0.95 (\pm 2.078)	-15.78 (\pm 6.252)	99999 (\pm 99999)	0.56 (\pm 6.129)
Change at Week 3 (n=10, 1, 0, 0 and 20)	-3.80 (\pm 2.848)	-12.39 (\pm 8.240)	99999 (\pm 99999)	99999 (\pm 99999)
Change at Week 4 (n=18, 7, 9, 9 and 37)	-6.28 (\pm 2.182)	-0.84 (\pm 3.940)	-2.48 (\pm 3.572)	-2.91 (\pm 3.575)
Change at Week 5 (n=18, 6, 6, 8 and 34)	-5.12 (\pm 2.386)	-6.14 (\pm 4.414)	3.10 (\pm 4.347)	-1.22 (\pm 3.935)

Change at Week 10 (n=17, 5, 2, 6 and 30)	-5.09 (± 1.967)	-2.21 (± 3.902)	5.77 (± 5.365)	-2.36 (± 3.607)
Change at Week 15 (n=8, 1, 1, 3 and 15)	-0.18 (± 3.170)	7.72 (± 8.660)	2.09 (± 9.495)	-5.44 (± 5.364)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Scale				
least squares mean (standard error)				
Change at Week 1 (n=21, 7, 9, 9 and 41)	-3.22 (± 1.524)			
Change at Week 2 (n=11, 1, 0, 1 and 20)	-3.70 (± 1.584)			
Change at Week 3 (n=10, 1, 0, 0 and 20)	-3.06 (± 2.069)			
Change at Week 4 (n=18, 7, 9, 9 and 37)	-6.05 (± 1.574)			
Change at Week 5 (n=18, 6, 6, 8 and 34)	-4.86 (± 1.765)			
Change at Week 10 (n=17, 5, 2, 6 and 30)	-9.32 (± 1.526)			
Change at Week 15 (n=8, 1, 1, 3 and 15)	-1.84 (± 2.519)			

Statistical analyses

No statistical analyses for this end point

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

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

The MDS-UPDRS included components assessed by the investigator as well as sections completed by the subject. Part I (Non-Motor Aspects of Experiences of daily Living) assessed non motor experiences of daily living (Score: 0-52); Part II (Motor Aspects of Experiences of Daily Living) assessed motor experiences of daily living. There were additional 13 questions that were also part of the Questionnaire completed by the subject (Score: 0-52); Part IV (Motor Complications) assessed motor complications, dyskinesias, and motor fluctuations using historical and objective information (Score: 0-24); MDS-UPDRS Total Score: The sum of Parts I, II, III, and IV. Full Analysis Set included all subjects randomized who completed at least 1 post-dose efficacy measurement (Hauser home diary). (n is number of subjects evaluable for each treatment arm) Results at Week 15 should be interpreted with caution given almost half the subjects were not available for this analysis as compared to Week 10.

End point type	Secondary
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End point timeframe:

Weeks 5, 10 and 15; Baseline was defined as the Day -1 (study derived day and equalled to nominal visit Day 0) measurement

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	7	9	9
Units: Scale				
arithmetic mean (standard deviation)				
Change at Week 5 (Part I) (n=16, 6, 6, 8, 34)	-0.75 (± 5.508)	-0.83 (± 1.941)	0.67 (± 4.885)	2.00 (± 4.408)
Change at Week 10 (Part I) (n=16, 5, 2, 6, 30)	-0.69 (± 4.557)	-0.80 (± 2.168)	-1.00 (± 2.828)	0.00 (± 2.449)
Change at Week 15 (Part I) (n=7, 1, 1, 3, 15)	-2.86 (± 6.176)	2.00 (± 99999)	6.00 (± 99999)	-1.00 (± 1.732)
Change at Week 5 (Part II) (n=18, 6, 6, 8, 34)	0.06 (± 5.836)	-1.83 (± 2.639)	3.00 (± 4.940)	-0.03 (± 3.083)
Change at Week 10 (Part II) (n=17, 5, 2, 6, 30)	-0.35 (± 5.267)	-1.00 (± 1.225)	5.00 (± 1.414)	0.13 (± 2.428)
Change at Week 15 (Part II) (n=8, 1, 1, 3, 15)	-1.38 (± 4.779)	2.00 (± 99999)	8.00 (± 99999)	-2.42 (± 5.270)
Change at Week 5 (Part IV) (n=18, 6, 6, 8, 34)	-1.50 (± 2.895)	-0.83 (± 2.401)	-0.50 (± 4.848)	0.25 (± 2.053)
Change at Week 10 (Part IV) (n=17, 5, 2, 6, 30)	-2.00 (± 2.318)	0.80 (± 1.304)	-3.00 (± 5.657)	0.00 (± 1.789)
Change at Week 15 (Part IV) (n=8, 1, 1, 3, 15)	-2.75 (± 2.493)	-2.00 (± 99999)	-7.00 (± 99999)	-1.33 (± 2.082)
Change at Week 5 (Total) (n=16, 6, 6, 8, 34)	-8.88 (± 12.832)	-10.00 (± 7.616)	5.33 (± 16.860)	2.34 (± 12.010)
Change at Week 10 (Total) (n=16, 5, 2, 6, 30)	-8.75 (± 10.951)	-3.60 (± 8.649)	6.50 (± 7.778)	0.13 (± 10.569)
Change at Week 15 (Total) (n=7, 1, 1, 3, 15)	-7.86 (± 12.456)	0.00 (± 99999)	13.00 (± 99999)	-9.08 (± 13.135)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Scale				
arithmetic mean (standard deviation)				
Change at Week 5 (Part I) (n=16, 6, 6, 8, 34)	1.12 (± 4.879)			
Change at Week 10 (Part I) (n=16, 5, 2, 6, 30)	0.17 (± 4.086)			
Change at Week 15 (Part I) (n=7, 1, 1, 3, 15)	1.00 (± 5.745)			
Change at Week 5 (Part II) (n=18, 6, 6, 8, 34)	-0.24 (± 4.068)			
Change at Week 10 (Part II) (n=17, 5, 2, 6, 30)	-0.43 (± 4.240)			
Change at Week 15 (Part II) (n=8, 1, 1, 3, 15)	1.47 (± 5.986)			
Change at Week 5 (Part IV) (n=18, 6, 6, 8, 34)	-0.65 (± 2.806)			
Change at Week 10 (Part IV) (n=17, 5, 2, 6, 30)	-1.13 (± 3.530)			
Change at Week 15 (Part IV) (n=8, 1, 1, 3, 15)	-1.27 (± 2.404)			
Change at Week 5 (Total) (n=16, 6, 6, 8, 34)	-4.21 (± 18.216)			

Change at Week 10 (Total) (n=16, 5, 2, 6, 30)	-11.40 (\pm 18.448)			
Change at Week 15 (Total) (n=7, 1, 1, 3, 15)	0.73 (\pm 17.260)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities Without Regard to Baseline Abnormality

End point title	Number of Subjects With Laboratory Abnormalities Without Regard to Baseline Abnormality
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End point description:

The safety laboratory tests including Hematology, Clinical Chemistry and Urinalysis were performed. Determination if there were any laboratory data abnormalities of potential clinical concern was based on Pfizer Data Standards.

Incidence of laboratory test abnormalities (without regard to baseline abnormality) was summarized within each treatment group.

Analysis population was Safety Analysis Set including all subjects who received at least 1 dose of PF-06649751 or placebo.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) to Week 17

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	15	13
Units: Subjects				
Number of subjects with laboratory abnormalities	19	4	9	7

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
Number of subjects with laboratory abnormalities	25			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Sign Results Meeting the Criteria for Categorical Summarization.

End point title	Number of Subjects With Vital Sign Results Meeting the Criteria for Categorical Summarization.
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End point description:

Vital Signs including blood pressure and pulse rate were measured.

Vital signs were collected first while the subject was in the supine position and then in the standing position. Analysis population was Safety Analysis Set including all subjects who received at least 1 dose of PF-06649751 or placebo.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) to Week 17

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	13	15	13
Units: Subjects				
<90 mmHg (Supine Systolic Blood Pressure [SBP])	1	1	2	0
Max-Increase from Baseline \geq 30 mmHg (Supine SBP)	4	1	2	1
Max-Decrease from Baseline \geq 30 mmHg (Supine SBP)	4	1	2	2
<90 mmHg (Standing SBP)	4	1	3	2
Max-Increase from Baseline \geq 30mmHg (Standing SBP)	4	0	3	1
Max-Decrease from Baseline \geq 30mmHg (Standing SBP)	3	0	3	2
<50 mmHg (Supine Diastolic Blood Pressure [DBP])	0	0	0	1
Max-Increase from Baseline \geq 20 mmHg (Supine DBP)	1	0	0	1
Max-Decrease from Baseline \geq 20 mmHg (Supine DBP)	1	0	2	1
<50 mmHg (Standing DBP)	2	0	1	2
Max-Increase from Baseline \geq 20mmHg (Standing DBP)	3	0	2	0
Max-Decrease from Baseline \geq 20mmHg (Standing DBP)	5	2	3	2
<40 beats per minute (bpm) (Supine Pulse Rate)	0	0	0	0
>120 bpm (Supine Pulse Rate)	0	0	0	0
<40 bpm (Standing Pulse Rate)	0	0	0	0
>140 bpm (Standing Pulse Rate)	0	0	0	0

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				

<90 mmHg (Supine Systolic Blood Pressure [SBP])	3			
Max-Increase from Baseline \geq 30 mmHg (Supine SBP)	3			
Max-Decrease from Baseline \geq 30 mmHg (Supine SBP)	11			
<90 mmHg (Standing SBP)	7			
Max-Increase from Baseline \geq 30mmHg (Standing SBP)	3			
Max-Decrease from Baseline \geq 30mmHg (Standing SBP)	12			
<50 mmHg (Supine Diastolic Blood Pressure [DBP])	1			
Max-Increase from Baseline \geq 20 mmHg (Supine DBP)	3			
Max-Decrease from Baseline \geq 20 mmHg (Supine DBP)	13			
<50 mmHg (Standing DBP)	1			
Max-Increase from Baseline \geq 20mmHg (Standing DBP)	1			
Max-Decrease from Baseline \geq 20mmHg (Standing DBP)	17			
<40 beats per minute (bpm) (Supine Pulse Rate)	0			
>120 bpm (Supine Pulse Rate)	0			
<40 bpm (Standing Pulse Rate)	0			
>140 bpm (Standing Pulse Rate)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Electrocardiogram (ECG) Results Meeting the Criteria for Categorical Summarization

End point title	Number of Subjects with Electrocardiogram (ECG) Results Meeting the Criteria for Categorical Summarization
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End point description:

The average of the triplicate readings of ECG data was collected at each assessment time. Number of subjects with ECG results meeting the criteria for categorical summarization for time from the beginning of the P wave until the beginning of the QRS complex (PR Interval), time from ECG Q wave to the end of the S wave corresponding to ventricle depolarization (QRS Duration), time between the start of the Q wave and the end of the T wave in the heart's electrical cycle (QT Interval) and corrected QT (Fridericia correction) (QTcF Interval) were presented. Analysis population was Safety Analysis Set including all subjects who received at least 1 dose of PF-06649751 or placebo.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) to Week 17

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	15	13
Units: Subjects				
>=300 msec (PR Interval)	1	0	0	0
Max-Increase From Baseline(%)>=25/50%(PR Interval)	0	0	0	0
>=140 msec (QRS Duration)	0	0	0	0
Max-Increase From Baseline(%)>=50% (QRS Duration)	0	0	0	0
>=500 msec (QT Interval)	1	0	0	0
450 - <480 msec (QTcF Interval)	2	0	0	0
480 - <500 msec (QTcF Interval)	0	0	0	0
>=500 msec (QTcF Interval)	0	0	0	0
Max-Increase From Baseline 30-<60 (QTcF Interval)	1	0	0	0
Max-Increase From Baseline >=60 (QTcF Interval)	0	0	0	0

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
>=300 msec (PR Interval)	0			
Max-Increase From Baseline(%)>=25/50%(PR Interval)	0			
>=140 msec (QRS Duration)	0			
Max-Increase From Baseline(%)>=50% (QRS Duration)	0			
>=500 msec (QT Interval)	0			
450 - <480 msec (QTcF Interval)	1			
480 - <500 msec (QTcF Interval)	0			
>=500 msec (QTcF Interval)	0			
Max-Increase From Baseline 30-<60 (QTcF Interval)	1			
Max-Increase From Baseline >=60 (QTcF Interval)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Suicidal Ideation Assessed Using the Columbia Suicide Severity Rating Scale (C-SSRS) at Post-baseline Visits

End point title	Number of Subjects With Suicidal Ideation Assessed Using the Columbia Suicide Severity Rating Scale (C-SSRS) at Post-baseline Visits
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End point description:

The Columbia Suicide Severity Rating Scale (C-SSRS) was an interview based rating scale to

systematically assess suicidal ideation and suicidal behavior. C-SSRS responses were mapped to the C-CASA. There were 3 key endpoints for suicidality data analysis and evaluation: Suicidal Behavior: A subject was said to have suicidal behavior if the subject had experienced completed suicide/suicide attempt/reparatory acts toward imminent suicidal behavior; Suicidal Ideation: Any observed suicidal ideation mapped to a single C-CASA category; Suicidal Behavior or Ideation (subjects with new onset suicidality): A subject was considered to have a new onset of suicidality if the subject reported no ideation and no behavior at the baseline assessment and reported any behavior or ideation post-baseline. Safety Analysis Set included all subjects who received at least 1 dose of PF-06649751 or placebo. (n in the following table stands for number of subjects evaluable for each treatment arm)

End point type	Secondary
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End point timeframe:

Days 0 (Baseline), 7, 14, 21, 28, 35, 70, 77, 84, 91, 105 and 119

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	13	15	13
Units: Subjects				
Baseline (n=23, 13, 15, 13 and 44)	1	0	1	0
Day 7 (n=22, 11, 14, 12 and 44)	0	0	0	0
Day 14 (n=19, 7, 10, 9 and 39)	0	0	0	0
Day 21 (n=21, 10, 10, 8 and 39)	0	0	0	0
Day 28 (n=19, 8, 9, 11 and 39)	0	0	0	0
Day 35 (n=21, 8, 7, 10 and 36)	0	0	0	0
Day 70 (n=20, 6, 7, 7 and 32)	0	0	0	0
Day 77 (n=6, 0, 0, 0 and 9)	0	0	0	0
Day 84 (n=7, 0, 0, 0 and 8)	0	0	0	0
Day 91 (n=6, 0, 0, 0 and 6)	0	0	0	0
Day 105 (n=17, 4, 3, 6 and 25)	0	0	0	1
Day 119 (n=15, 1, 0, 3 and 25)	0	0	0	0

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
Baseline (n=23, 13, 15, 13 and 44)	0			
Day 7 (n=22, 11, 14, 12 and 44)	0			
Day 14 (n=19, 7, 10, 9 and 39)	1			
Day 21 (n=21, 10, 10, 8 and 39)	2			
Day 28 (n=19, 8, 9, 11 and 39)	0			
Day 35 (n=21, 8, 7, 10 and 36)	1			
Day 70 (n=20, 6, 7, 7 and 32)	0			
Day 77 (n=6, 0, 0, 0 and 9)	0			
Day 84 (n=7, 0, 0, 0 and 8)	0			
Day 91 (n=6, 0, 0, 0 and 6)	0			
Day 105 (n=17, 4, 3, 6 and 25)	0			
Day 119 (n=15, 1, 0, 3 and 25)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Questionnaire for Impulsive-Compulsive Disorders (ICDs) in Parkinson's Disease – Rating Scale (QUIP-RS)

End point title	Change From Baseline in Total Questionnaire for Impulsive-Compulsive Disorders (ICDs) in Parkinson's Disease – Rating Scale (QUIP-RS)
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End point description:

The QUIP-RS was a brief, patient reported outcome measure designed to assess the severity of symptoms of ICDs and related behaviors reported to occur in Parkinson's disease. The QUIP-RS assesses 7 disorders (Gambling, Sex, Buying, Eating, Hobbyism-punding [performing tasks and repeating activities] and Taking medications), and the higher score indicated a greater level of the ICD. The total QUIP-RS score for all ICDs and related disorders combined ranges from 0 to 112.

Safety Analysis Set included all subjects who received at least 1 dose of PF-06649751 or placebo. (n in the following table stands for number of subjects evaluable for each treatment arm)

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Weeks 5, 10 and 15

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	13	15	13
Units: Scale				
arithmetic mean (standard deviation)				
Baseline (n=23, 13, 15, 13 and 44)	17.1 (± 16.98)	9.0 (± 12.56)	9.0 (± 14.39)	12.5 (± 11.69)
Change at Week 5 (n=22, 11, 10, 12 and 42)	-5.6 (± 11.37)	2.3 (± 10.05)	4.7 (± 9.58)	-5.4 (± 12.28)
Change at Week 10 (n=20, 5, 6, 6 and 30)	-3.3 (± 12.16)	-1.8 (± 7.98)	-6.5 (± 9.63)	-5.8 (± 13.50)
Change at Week 15 (n=16, 4, 3, 4 and 24)	-11.5 (± 16.29)	3.0 (± 10.30)	-3.3 (± 5.77)	-17.0 (± 11.34)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Scale				
arithmetic mean (standard deviation)				
Baseline (n=23, 13, 15, 13 and 44)	6.8 (± 11.40)			
Change at Week 5 (n=22, 11, 10, 12 and 42)	0.5 (± 11.13)			

Change at Week 10 (n=20, 5, 6, 6 and 30)	1.0 (\pm 10.62)			
Change at Week 15 (n=16, 4, 3, 4 and 24)	0.4 (\pm 5.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Physician Withdrawal Checklist (PWC-20) on Days 105 and 119, and Change From Day 105 to Day 119

End point title	Total Physician Withdrawal Checklist (PWC-20) on Days 105 and 119, and Change From Day 105 to Day 119
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End point description:

The PWC-20 is a physician completed, 20 item reliable and sensitive instrument for the assessment of discontinuation symptoms. The PWC-20 was collected after the completion of study treatment and also at the first visit of follow-up.

The total PWC-20 score was the sum of 20 item scores and ranged from 0 to 60, and the higher score indicated more frequent/severe symptoms.

Analysis population was Safety Analysis Set including all subjects who received at least 1 dose of PF-06649751 or placebo.

(n in the following table stands for number of subjects evaluable for each treatment arm)

End point type	Secondary
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End point timeframe:

Days 105 and 119

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	13	15	13
Units: Scale				
arithmetic mean (standard deviation)				
Day 105 (n=22, 12, 13, 13 and 40)	3.5 (\pm 3.73)	5.6 (\pm 5.68)	5.8 (\pm 6.65)	8.2 (\pm 8.78)
Day 119 (n=15, 1, 0, 3 and 25)	3.3 (\pm 3.08)	6.0 (\pm 99999)	99999 (\pm 99999)	7.7 (\pm 4.16)
Change From Day 105 to 119 (n=14, 1, 0, 3 and 24)	-0.6 (\pm 3.08)	-11.0 (\pm 99999)	99999 (\pm 99999)	-1.7 (\pm 4.73)

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Scale				
arithmetic mean (standard deviation)				
Day 105 (n=22, 12, 13, 13 and 40)	7.1 (\pm 6.06)			
Day 119 (n=15, 1, 0, 3 and 25)	5.8 (\pm 5.45)			
Change From Day 105 to 119 (n=14, 1, 0, 3 and 24)	-0.4 (\pm 4.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), Discontinuation due to AEs and Deaths

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), Discontinuation due to AEs and Deaths
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End point description:

An AE was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not need necessarily to have a causal relationship with the treatment or usage.

An SAE was any untoward medical occurrence at any dose that:

- Resulted in death;
- Was life threatening (immediate risk of death);
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);
- Resulted in congenital anomaly/birth defect.

Analysis population was Safety Analysis Set including all subjects who received at least 1 dose of PF-06649751 or placebo.

End point type	Secondary
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End point timeframe:

Day 1 to follow-up (Week 19 visit)

End point values	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD	PF-06649751 7 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	13	15	13
Units: Subjects				
AEs	20	7	11	10
SAEs	1	1	0	0
Discontinuation due to AEs	3	1	3	2
Death	1	0	0	0

End point values	PF-06649751 15 mg QD			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Subjects				
AEs	37			
SAEs	2			
Discontinuation due to AEs	9			

Death	1			
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to follow-up (Week 19 visit)

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	Placebo
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Reporting group description:

The subjects swallowed 3 tablets once daily (QD) at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks. A follow-up visit was at Week 17, 2 weeks after discontinuation of Placebo. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 1 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 3 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Reporting group title	PF-06649751 7 mg QD
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Reporting group description:

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

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

The subjects swallowed 3 tablets QD at approximately the same time each morning within approximately 5 minutes without being manipulated or chewed prior to being swallowed. Duration of treatment was 15 weeks including: 3-week titration of PF-06649751 administered QD to the randomized target dose; 2-week stabilization period for dose adjustment after reaching the target dose; 5-week Period A of PF-06649751 administered QD adjunctive to stable doses of L-Dopa; 5-week Period B (maintenance period) of PF-06649751 administered QD adjunctive to stable doses of L-Dopa. A follow-up visit was at Week 17, 2 weeks after discontinuation of PF-06649751. A follow-up phone visit was scheduled at Week 19 for subject's safety.

Serious adverse events	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 23 (4.35%)	1 / 13 (7.69%)	0 / 15 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (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
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			

subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (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
Pain in extremity			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (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	PF-06649751 7 mg QD	PF-06649751 15 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	2 / 44 (4.55%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Dermatitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	PF-06649751 1 mg QD	PF-06649751 3 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 23 (65.22%)	7 / 13 (53.85%)	11 / 15 (73.33%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hot flush			

subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Orthostatic hypotension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 23 (13.04%)	1 / 13 (7.69%)	2 / 15 (13.33%)
occurrences (all)	3	1	2
Malaise			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 23 (4.35%)	1 / 13 (7.69%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Aggression			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Anxiety			

subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Delusion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Depersonalisation/derealisation disorder			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dysphemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypersexuality			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	3 / 23 (13.04%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	3	1	0
Irritability			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rapid eye movement sleep behaviour disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Investigations			

Blood pressure decreased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0
Urine output decreased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0
Injury, poisoning and procedural complications			
Bone contusion subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 13 (7.69%) 1	0 / 15 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	2 / 13 (15.38%) 2	1 / 15 (6.67%) 1
Joint injury subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1
Laceration subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 13 (7.69%) 1	0 / 15 (0.00%) 0
Skin abrasion subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0
Cardiac disorders			
Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1
Nervous system disorders			
Balance disorder subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1

Dyskinesia			
subjects affected / exposed	2 / 23 (8.70%)	1 / 13 (7.69%)	1 / 15 (6.67%)
occurrences (all)	2	2	1
Dystonia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Headache			
subjects affected / exposed	0 / 23 (0.00%)	2 / 13 (15.38%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Memory impairment			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Parkinson's disease			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 23 (4.35%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysphagia			

subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	2 / 13 (15.38%)	2 / 15 (13.33%)
occurrences (all)	1	2	2
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Posture abnormal			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Chronic sinusitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	3 / 23 (13.04%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	4	0	0
Tooth abscess			
subjects affected / exposed	1 / 23 (4.35%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 23 (4.35%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	PF-06649751 7 mg QD	PF-06649751 15 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 13 (76.92%)	31 / 44 (70.45%)	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Orthostatic hypotension			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 44 (4.55%) 2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Fatigue			
subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	1 / 44 (2.27%) 1	
Malaise			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Pyrexia			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	3 / 44 (6.82%) 4	
Aggression			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Anxiety			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	3 / 44 (6.82%) 3	
Delusion			
subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Depersonalisation/derealisation disorder			
subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	

Depression			
subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Dysphemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Hypersexuality			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Irritability			
subjects affected / exposed	0 / 13 (0.00%)	4 / 44 (9.09%)	
occurrences (all)	0	4	
Rapid eye movement sleep behaviour disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	2	
Investigations			
Blood pressure decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Urine output decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Contusion			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	0 / 44 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	2 / 44 (4.55%) 3	
Joint injury subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Laceration subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Skin abrasion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 44 (2.27%) 1	
Cardiac disorders Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	4 / 44 (9.09%) 4	
Dyskinesia subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	7 / 44 (15.91%) 7	
Dystonia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Headache subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	11 / 44 (25.00%) 14	
Memory impairment			

subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Myoclonus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Parkinson's disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Dysphagia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 44 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 13 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	11 / 44 (25.00%)	
occurrences (all)	1	14	

Vomiting subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 44 (4.55%) 2	
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Musculoskeletal and connective tissue disorders Flank pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 44 (2.27%) 1	
Neck pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Posture abnormal subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Infections and infestations Asymptomatic bacteriuria subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Chronic sinusitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 44 (0.00%) 0	

Tooth abscess subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 44 (0.00%) 0	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 44 (6.82%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 July 2016	<ul style="list-style-type: none">• Clarified that primary and secondary endpoints were measured in ON and OFF "hours";• Added "Daily ON Time with troublesome dyskinesia (hours)" as a secondary endpoint;• Clarified that secondary endpoints were measured as change from baseline;• Added cognition as an exploratory objective;• Added SDMT as an exploratory endpoint for cognition;• Added electronic Parkinson's disease Activity of Daily Living and Improvement (ADL&I) Scale as an optional exploratory sub study in a subset of subjects (US sites only).
22 November 2016	<ul style="list-style-type: none">• Removed "reduction of L-Dopa dose" from the secondary objectives;• Removed secondary endpoints related to daily L-Dopa dose;• L-Dopa reduction was no longer required during Period B and daily L-Dopa dose and frequency should remain stable over the entire course of the study (except in the case of unacceptable dopaminergic AEs);• Required clinic visits and corresponding MDS-UPDRS III deleted at Week 2, Week 3, Week 11, Week 12 and Week 13;• Added the open-label extension study.
17 July 2017	France only: The protocol underwent a country-specific amendment at the request of the France Regulatory Authorities to include guidance for the eye examination.

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.

The study was terminated prematurely due to insufficient efficacy and not due to safety reasons.

Notes: