Clinical trial results:
A Phase 2, Randomized, Placebo Controlled, Double Blind Proof-of-Concept Study of the Efficacy and Safety of PF-02545920 in Subjects With Huntington's Disease

Summary

EudraCT number	2014-001291-56
Trial protocol	DE GB
Global end of trial date	04 October 2016

Results information

Result version number	v1 (current)
This version publication date	23 September 2017
First version publication date	23 September 2017

Trial information

Trial identification

Sponsor protocol code	A8241021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02197130
WHO universal trial number (UTN)	-
Other trial identifiers	The Amaryllis Study: Alias

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 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	30 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 September 2016
Global end of trial reached?	Yes
Global end of trial date	04 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of 26-week oral daily dosing with PF-02545920 on motor function in subjects with Huntington'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 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: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2014
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: 17
Country: Number of subjects enrolled	Germany: 88
Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	United Kingdom: 69
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	272
EEA total number of subjects	188

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)	268
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 272 subjects (133 males and 139 females) were randomized and assigned study treatment, of which 270 subjects received their treatments from the baseline.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-02545920 20 mg BID

Arm description:

The 20 mg BID dose of PF-02545920 was titrated as follows: 5 mg BID for 7 days, 10 mg BID for 7 days, 15 mg BID for 7 days, then 20 mg BID for the remainder of the treatment phase. Participants took 4 tablets packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. The blister packs contained 3 placebo tablets and one 5 mg PF-02545920 tablet for Days 1-7, 2 placebo tablets and two 5 mg PF-02545920 tablets for Days 8-14, 1 placebo tablet and three 5 mg PF-02545920 tablets for Days 15-21, and four 5 mg PF-02545920 tablets from Day 22 through Day 182. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Arm type	Experimental
Investigational medicinal product name	PF-02545920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The 20 mg BID dose of PF-02545920 was titrated as follows: 5 mg BID for 7 days, 10 mg BID for 7 days, 15 mg BID for 7 days, then 20 mg BID for the remainder of the treatment phase. Subjects took 4 tablets packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. The blister packs contained 3 placebo tablets and one 5 mg PF-02545920 tablet for Days 1-7, 2 placebo tablets and two 5 mg PF-02545920 tablets for Days 8-14, 1 placebo tablet and three 5 mg PF-02545920 tablets for Days 15-21, and four 5 mg PF-02545920 tablets from Day 22 through Day 182. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Arm title	PF-02545920 5 mg BID

Arm description:

Participants took 4 tablets packaged in blister packs (3 placebo tablets and one 5 mg PF-02545920) twice a day approximately every 12 hours from Baseline Day 1 (V2) to Week 26 (V9), at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Arm type	Experimental
Investigational medicinal product name	PF-02545920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects took 4 tablets packaged in blister packs (3 placebo tablets and one 5 mg PF-02545920) twice a day approximately every 12 hours from Baseline Day 1 (V2) to Week 26 (V9), at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Arm title	Placebo

Arm description:

Participants took 4 tablets of placebo packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

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:

Subjects took 4 tablets of placebo packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Number of subjects in period 1	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo
Started	88	95	89
Received treatment	87	95	88
Completed	56	79	81
Not completed	32	16	8
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	4	-	3
Does not meet entrance criteria	1	-	-
Adverse event, non-fatal	23	13	4
Unspecified	3	1	-
Lost to follow-up	1	2	-

Baseline characteristics

Reporting groups	
Reporting group title	PF-02545920 20 mg BID

Reporting group description:

The 20 mg BID dose of PF-02545920 was titrated as follows: 5 mg BID for 7 days, 10 mg BID for 7 days, 15 mg BID for 7 days, then 20 mg BID for the remainder of the treatment phase. Participants took 4 tablets packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. The blister packs contained 3 placebo tablets and one 5 mg PF-02545920 tablet for Days 1-7, 2 placebo tablets and two 5 mg PF-02545920 tablets for Days 8-14, 1 placebo tablet and three 5 mg PF-02545920 tablets for Days 15-21, and four 5 mg PF-02545920 tablets from Day 22 through Day 182. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	PF-02545920 5 mg BID

Reporting group description:

Participants took 4 tablets packaged in blister packs (3 placebo tablets and one 5 mg PF-02545920) twice a day approximately every 12 hours from Baseline Day 1 (V2) to Week 26 (V9), at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	Placebo

Reporting group description:

Participants took 4 tablets of placebo packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo
Number of subjects	88	95	89
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	86	93	89
From 65-84 years	2	2	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	48.3	48.3	50.3
standard deviation	± 9.2	± 8.6	± 9.4
Gender, Male/Female Units: Subjects			
Female	43	42	54
Male	45	53	35

Reporting group values	Total		
Number of subjects	272		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	268		
From 65-84 years	4		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Subjects			
Female	139		
Male	133		

End points

End points reporting groups

Reporting group title	PF-02545920 20 mg BID

Reporting group description:

The 20 mg BID dose of PF-02545920 was titrated as follows: 5 mg BID for 7 days, 10 mg BID for 7 days, 15 mg BID for 7 days, then 20 mg BID for the remainder of the treatment phase. Participants took 4 tablets packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. The blister packs contained 3 placebo tablets and one 5 mg PF-02545920 tablet for Days 1-7, 2 placebo tablets and two 5 mg PF-02545920 tablets for Days 8-14, 1 placebo tablet and three 5 mg PF-02545920 tablets for Days 15-21, and four 5 mg PF-02545920 tablets from Day 22 through Day 182. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	PF-02545920 5 mg BID

Reporting group description:

Participants took 4 tablets packaged in blister packs (3 placebo tablets and one 5 mg PF-02545920) twice a day approximately every 12 hours from Baseline Day 1 (V2) to Week 26 (V9), at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	Placebo

Reporting group description:

Participants took 4 tablets of placebo packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Primary: Change from Baseline in the Total Motor Score (TMS) Assessment of the Unified Huntington Disease Rating Scale (UHDRS) After 26 Weeks of Treatment.

End point title	Change from Baseline in the Total Motor Score (TMS) Assessment of the Unified Huntington Disease Rating Scale (UHDRS) After 26 Weeks of Treatment.

End point description:

The UHDRS is a clinical rating scale which has been developed by the Huntington Disease Study Group (HSG) to provide a uniform assessment of the clinical features and course of Huntington's Disease (HD). The components of the full UHDRS assess motor function, cognition, behavior and functional abilities. The total motor score (TMS) assessed motor features of HD with standardized ratings of oculomotor function, dysarthria, chorea, dystonia, gait, and postural stability. Some items (such as chorea and dystonia) required grading each extremity (face, bucco-oral-lingual, and trunk) separately. Eye movements require both horizontal and vertical grades. The total motor impairment scores is the sum of all the individual motor ratings, with higher scores indicating more severe motor impairment than lower scores.

End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	83	80	
Units: units on a scale				
arithmetic mean (standard deviation)	0.4 (± 8.63)	-0.8 (± 7.3)	-1.4 (± 6.67)	

Statistical analyses

Statistical analysis title	Change from Baseline in TMS Assessment of UHDRS
Statistical analysis description: Baseline, Week 26	
Comparison groups	PF-02545920 20 mg BID v Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2033
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.45
upper limit	3.49
Variability estimate	Standard error of the mean
Dispersion value	1.192

Statistical analysis title	Change from Baseline in TMS Assessment of UHDRS
Statistical analysis description: Baseline, Week 26	
Comparison groups	PF-02545920 5 mg BID v Placebo
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7549
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.2
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	1.118

Secondary: Number of Subjects that Met White Blood Count (WBC) and Absolute Neutrophil Count (ANC) Stopping Criteria

End point title	Number of Subjects that Met White Blood Count (WBC) and Absolute Neutrophil Count (ANC) Stopping Criteria

End point description:

The criteria for temporary study suspension was as follow: Criterion A: WBC count <=3000 cells/mm3 but >= 2000 cells/mm3 or ANC <= 1500 cells/mm3 but >= 1000 cells/mm3; Criterion B: WBC <= 2000 cells/mm3 or ANC <= 1000 cells/mm3; Criterion C: participants who are discontinued or permanently suspended due to WBC or ANC findings; Criterion D: ANC <= 500 cells/mm3

End point type	Secondary

End point timeframe:

Screening, Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects				
Criterion A	0	1	0	
Criterion B	0	0	0	
Criterion C	0	0	0	
Criterion D	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events

End point title	Number of Subjects with Adverse Events

End point description:

Adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship.

End point type	Secondary

End point timeframe:

Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects	76	82	63	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Serious Adverse Events

End point title	Number of Subjects with Serious Adverse Events

End point description:

Adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death, initial or prolonged inpatient hospitalization, life-threatening experience (immediate risk of dying), persistent or significant disability or incapacity, congenital anomaly.

End point type	Secondary

End point timeframe:

Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects	8	2	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Test Abnormalities (Without Regard to Baseline Abnormalities)

End point title	Number of Subjects with Laboratory Test Abnormalities (Without Regard to Baseline Abnormalities)

End point description:

Following parameters were analyzed for laboratory examination: hematology (hemoglobin, hematocrit, red blood cell count, platelet count, white blood cell count, total neutrophils, eosinophils, monocytes, basophils, lymphocytes);coagulation (PT international ratio); liver function (total bilirubin, direct bilirubin, indirect bilirubin, aspartate aminotransferase, alanine aminotransferase, gamma GT, LDH, alkaline phosphatase, total protein, albumin); renal function (blood urea nitrogen, creatinine, uric acid); electrolytes (calcium, sodium, potassium, chloride, total bicarbonate, magnesium, phosphate); clinical chemistry (glucose, glycosylated, hemoglobin, human chorionic gonadotropin, creatine kinase); urinalysis (decimal logarithm of reciprocal of hydrogen ion activity [pH], urine specific gravity, glucose, protein, blood, ketones, nitrite).

End point type	Secondary

End point timeframe:

Screening, Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	95	88	
Units: subjects	47	46	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Test Abnormalities (With Normal Baseline)

End point title	Number of Subjects with Laboratory Test Abnormalities (With Normal Baseline)

End point description:

Following parameters were analyzed for laboratory examination: hematology (hemoglobin, hematocrit, red blood cell count, platelet count, white blood cell count, total neutrophils, eosinophils, monocytes, basophils, lymphocytes);coagulation (PT international ratio); liver function (total bilirubin, direct bilirubin, indirect bilirubin, aspartate aminotransferase, alanine aminotransferase, gamma GT, LDH, alkaline phosphatase, total protein, albumin); renal function (blood urea nitrogen, creatinine, uric acid); electrolytes (calcium, sodium, potassium, chloride, total bicarbonate, magnesium, phosphate); clinical chemistry (glucose, glycosylated, hemoglobin, human chorionic gonadotropin, creatine kinase); urinalysis (decimal logarithm of reciprocal of hydrogen ion activity [pH], urine specific gravity, glucose, protein, blood, ketones, nitrite).

End point type	Secondary

End point timeframe:

Screening, Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	95	88	
Units: subjects	40	36	41	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Absolute Values)

End point title	Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Absolute Values)

End point description:

Absolute values were analyzed for supine systolic blood pressure (SBP), standing SBP, supine diastolic blood pressure (DBP), standing DBP, supine pulse rate, and standing pulse rate. Number of participants with vital signs data meeting the following criteria was reported: Criterion A: supine SBP less than (<) 90 millimeter of mercury(mmHg); Criterion B: standing SBP < 90 mmHg; Criterion C: supine DBP <50 mmHg; Criterion D: standing DBP <50 mmHg; Criterion E: supine pulse rate < 40 beats per minute(BPM); Criterion F: supine pulse rate greater than (>)120 BPM; Criterion G: standing pulse rate

beats per minute(BPM); Criterion H: standing pulse rate >120 BPM;

End point type	Secondary

End point timeframe:

Screening, Day 1, 28, 91, and 182

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects				
Criterion A	1	0	0	
Criterion B	3	2	3	
Criterion C	2	1	1	
Criterion D	1	3	0	
Criterion E	0	0	0	
Criterion F	0	0	1	
Criterion G	0	0	0	
Criterion H	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Increase from Baseline)

End point title	Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Increase from Baseline)

End point description:

The number of participants with vital signs data of maximum increase from baseline meeting the following criteria was reported: Criterion A: maximum increase from baseline in supine SBP greater than or equal to (>=) 30 mmHg; Criterion B: maximum increase from baseline in standing SBP >= 30 mmHg; Criterion C: maximum increase from baseline in supine DBP >=20 mmHg; Criterion D: maximum increase from baseline in standing DBP >=20 mmHg

End point type	Secondary

End point timeframe:

Screening, Day 1, 28, 91, and 182

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects				
Criterion A	4	1	4	
Criterion B	7	8	6	
Criterion C	3	3	10	
Criterion D	3	8	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Decrease from Baseline)

End point title	Number of Subjects with Vital Sign Data that Met Criteria for Potential Clinical Concern (Decrease from Baseline)

End point description:

The number of subjects with vital signs data of maximum decrease from baseline meeting the following criteria was reported: Criterion A: maximum decrease from baseline in supine SBP >= 30 mmHg; Criterion B: maximum decrease from baseline in standing SBP >= 30 mmHg; Criterion C: maximum decrease from baseline in supine DBP >=20 mmHg; Criterion D: maximum decrease from baseline in standing DBP >=20 mmHg

End point type	Secondary

End point timeframe:

Screening, Day 1, 28, 91, and 182

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects				
Criterion A	1	7	3	
Criterion B	9	8	9	
Criterion C	8	6	8	
Criterion D	10	14	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Electrocardiogram (ECG) Data that Met Criteria for Potential Clinical Concern(Absolute Values)

End point title	Number of Subjects with Electrocardiogram (ECG) Data that Met Criteria for Potential Clinical Concern(Absolute Values)

End point description:

The number of subjects with ECG absolute values meeting the following criteria was reported: Criterion A: maximum 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) >=300 msec; Criterion B: maximum QRS complex(time from Q wave to the end of S wave, corresponding to ventricle depolarization) >=140 msec; Criterion C: maximum QTcF interval (time from the beginning of Q wave to the end of T wave corresponding to electrical systole, corrected for heart rate using Fridericia's formula) 450-<480 msec; Criterion D: maximum QTcF interval 480-<500 msec; Criterion E: maximum

QTcF interval (Fridericia’s correction) >=500 msec

End point type	Secondary

End point timeframe:

Screening, Day 1, 28, 91, and 182

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	93	88	
Units: subjects				
Criterion A	0	0	0	
Criterion B	0	0	0	
Criterion C	5	2	7	
Criterion D	0	0	0	
Criterion E	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Electrocardiogram (ECG) Data that Met Criteria for Potential Clinical Concern(Increase from Baseline)

End point title	Number of Subjects with Electrocardiogram (ECG) Data that Met Criteria for Potential Clinical Concern(Increase from Baseline)

End point description:

Number of subjects with ECG meeting the following criteria was reported: Criterion A: maximum PR interval increase from baseline percentage change (PctChg)>= 25/50%; Criterion B: maximum QRS complex increase from baseline PctChg >=50%; Criterion C: maximum QTcF interval (Fridericia's correction) increase from baseline 30<=change<60 msec; Criterion D: maximum QTcF interval (Fridericia's correction) increase from baseline change >=60 msec.

End point type	Secondary

End point timeframe:

Screening, Day 1, 28, 91, and 182

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	93	88	
Units: subjects				
Criterion A	0	0	0	
Criterion B	0	0	0	
Criterion C	4	4	6	
Criterion D	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Adverse Events Related to Extrapyramidal Symptoms (EPS) Including Dystonia and Akathisia

End point title	Severity of Adverse Events Related to Extrapyramidal Symptoms (EPS) Including Dystonia and Akathisia

End point description:

Adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AE was assessed according to severity; mild (not causing any significant problem, dose adjustment not required), moderate (caused problem that does not interfere significantly with usual activities or the clinical status, dose adjustment needed due to adverse event) and severe (caused problem that interferes significantly with usual activities or the clinical status, study drug stopped due to adverse event). EPS were reported AEs of dystonia and akathisia.

End point type	Secondary

End point timeframe:

Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: participants				
Dystonia(Mild)	0	0	0	
Dystonia(Moderate)	0	0	0	
Dystonia(Severe)	1	0	0	
Akathisia(Mild)	1	2	0	
Akathisia(Moderate)	2	1	0	
Akathisia(Severe)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Total Maximum Chorea (TMC) Score of the UHDRS After 13 and 26 Weeks of Treatment.

End point title	Change from Baseline in the Total Maximum Chorea (TMC) Score of the UHDRS After 13 and 26 Weeks of Treatment.

End point description:

The UHDRS was a clinical rating scale which has been developed by the Huntington Disease Study Group (HSG) to provide a uniform assessment of the clinical features and course of HD. The components of the full UHDRS assess motor function, cognition, behavior and functional abilities. The Total Maximum

Chorea (TMC) was a subset of the TMS assessment. It was composed of the scoring of 7 chorea assessments (face, orobuccolingual, trunk, right and left upper extremities, right and left lower extremities). Each assessment was rated from 0 to 4 (absent to prolonged). n is the number of evaluable subjects in each visit.

End point type	Secondary

End point timeframe:

Baseline, Week 13, Week 26

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	95	88	
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 13 (n= 67, 83, 77)	1.1 (± 3.92)	-0.2 (± 3.5)	-0.9 (± 2.56)	
Week 26 (n=59, 83, 80)	0.7 (± 3.81)	-0.4 (± 2.84)	-0.8 (± 2.79)	

Statistical analyses

Statistical analysis title	Change from Baseline in TMC Score of the UHDRS

Statistical analysis description:

Baseline, Week 13

Comparison groups	PF-02545920 20 mg BID v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.69
upper limit	2.39
Variability estimate	Standard error of the mean
Dispersion value	0.515

Statistical analysis title	Change from Baseline in TMC Score of the UHDRS

Statistical analysis description:

Baseline, Week 13

Comparison groups	PF-02545920 5 mg BID v Placebo

Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4656
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.45
upper limit	1.17
Variability estimate	Standard error of the mean
Dispersion value	0.491

Statistical analysis title	Change from Baseline in TMC Score of the UHDRS
Statistical analysis description:	
Baseline, Week 26	
Comparison groups	PF-02545920 20 mg BID v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0149
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.39
upper limit	2.02
Variability estimate	Standard error of the mean
Dispersion value	0.492

Statistical analysis title	Change from Baseline in TMC Score of the UHDRS
Statistical analysis description:	
Baseline, Week 26	
Comparison groups	PF-02545920 5 mg BID v Placebo
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8233
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.1

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.66
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Number of Subjects with Suicidal Ideation or Suicidal Behavior as Assessed by the Columbia Suicide Severity Rating Scale (C-SSRS) from Baseline to Follow-up Visit

End point title	Number of Subjects with Suicidal Ideation or Suicidal Behavior as Assessed by the Columbia Suicide Severity Rating Scale (C-SSRS) from Baseline to Follow-up Visit

End point description:

The C-SSRS captured the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. C-SSRS assessed whether subject experienced following: completed suicide; suicide attempt; preparatory acts towards imminent suicidal behavior; suicidal ideation; self-injurious behavior, no suicidal intent. The results presented are the number of subjects with completed suicide or non-fatal suicide events or behaviors. Worsening of suicidal ideation was an increase in severity of suicidal ideation from baseline.

End point type	Secondary

End point timeframe:

Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	95	88	
Units: subjects				
Completed Suicide	0	0	0	
Suicide Attempt	1	0	0	
Imminent Suicidal Behavior	1	1	0	
Suicidal Ideation	7	5	4	
Self-Injurious Behavior, No Suicidal Attempt	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Improvement (CGI-I) Scale Score After 13 and 26 Weeks of Treatment.

End point title	Clinical Global Impression of Improvement (CGI-I) Scale Score After 13 and 26 Weeks of Treatment.

End point description:

CGI-I: 7-point clinician rated scale ranging from 1 (very much improved) to 7 (very much worse).

Clinician responded to a question: "Compared to your subject's condition at the beginning of treatment, how much has your subject changed?". Improvement was compared to baseline and was defined as a score of 1 (very much improved), 2 (much improved), or 3 (minimally improved) on the scale. Higher score = more affected. n is the number of evaluable subjects in each visit.

End point type	Secondary

End point timeframe:

Week 13 & Week 26

End point values	PF-02545920 20 mg BID	PF-02545920 5 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	95	88	
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 13 (n= 66, 83, 77)	4 (± 1)	3.7 (± 0.9)	3.6 (± 0.83)	
Week 26 (n=59, 83, 80)	3.9 (± 1.13)	3.8 (± 0.99)	3.8 (± 0.91)	

Statistical analyses

Statistical analysis title	CGI-I Scale Score

Statistical analysis description:

Week 13

Comparison groups	PF-02545920 20 mg BID v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0181
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.11
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.148

Statistical analysis title	CGI-I Scale Score

Statistical analysis description:

Week 13

Comparison groups	PF-02545920 5 mg BID v Placebo

Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7133
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.18
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	CGI-I Scale Score
Statistical analysis description:	
Week 26	
Comparison groups	PF-02545920 20 mg BID v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4657
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.15
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.163

Statistical analysis title	CGI-I Scale Score
Statistical analysis description:	
Week 26	
Comparison groups	PF-02545920 5 mg BID v Placebo
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8339
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.03

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.22
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.15

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1, 7, 14, 28, 56, 91, 133, 182 and follow-up visits (from Day 189 to 192)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	PF-02545920 5 mg BID

Reporting group description:

Subjects took 4 tablets packaged in blister packs (3 placebo tablets and one 5 mg PF-02545920) twice a day approximately every 12 hours from Baseline Day 1 (V2) to Week 26 (V9), at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	Placebo

Reporting group description:

Subjects took 4 tablets of placebo packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Reporting group title	PF-02545920 20 mg BID

Reporting group description:

The 20 mg BID dose of PF-02545920 was titrated as follows: 5 mg BID for 7 days, 10 mg BID for 7 days, 15 mg BID for 7 days, then 20 mg BID for the remainder of the treatment phase. Subjects took 4 tablets packaged in blister packs twice a day approximately every 12 hours, at approximately the same time of day throughout the study. The blister packs contained 3 placebo tablets and one 5 mg PF-02545920 tablet for Days 1-7, 2 placebo tablets and two 5 mg PF-02545920 tablets for Days 8-14, 1 placebo tablet and three 5 mg PF-02545920 tablets for Days 15-21, and four 5 mg PF-02545920 tablets from Day 22 through Day 182. Study medication was swallowed whole, and was not manipulated or chewed prior to swallowing.

Serious adverse events	PF-02545920 5 mg BID	Placebo	PF-02545920 20 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 95 (2.11%)	7 / 88 (7.95%)	8 / 87 (9.20%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Pancreatic carcinoma			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Head injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Rib fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 88 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular migraine			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
General disorders and administration site conditions			
General physical health deterioration			

subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Agitation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 88 (0.00%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	1 / 95 (1.05%)	1 / 88 (1.14%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal behaviour			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Suicidal ideation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Pneumonia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	0 / 87 (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
Urinary tract infection			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 95 (0.00%)	0 / 88 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	PF-02545920 5 mg BID	Placebo	PF-02545920 20 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 95 (74.74%)	42 / 88 (47.73%)	65 / 87 (74.71%)
Investigations			
Weight decreased			
subjects affected / exposed	6 / 95 (6.32%)	1 / 88 (1.14%)	15 / 87 (17.24%)
occurrences (all)	6	1	16
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	15 / 95 (15.79%)	9 / 88 (10.23%)	5 / 87 (5.75%)
occurrences (all)	30	16	10
Nervous system disorders			
Chorea			
subjects affected / exposed	4 / 95 (4.21%)	1 / 88 (1.14%)	8 / 87 (9.20%)
occurrences (all)	4	1	9
Dizziness			
subjects affected / exposed	1 / 95 (1.05%)	4 / 88 (4.55%)	10 / 87 (11.49%)
occurrences (all)	1	5	13
Dyskinesia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 88 (1.14%)	9 / 87 (10.34%)
occurrences (all)	0	1	12
Headache			
subjects affected / exposed	8 / 95 (8.42%)	8 / 88 (9.09%)	8 / 87 (9.20%)
occurrences (all)	10	15	15
Sedation			
subjects affected / exposed	5 / 95 (5.26%)	0 / 88 (0.00%)	2 / 87 (2.30%)
occurrences (all)	6	0	2
Somnolence			
subjects affected / exposed	9 / 95 (9.47%)	3 / 88 (3.41%)	16 / 87 (18.39%)
occurrences (all)	12	3	20
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 95 (11.58%)	9 / 88 (10.23%)	16 / 87 (18.39%)
occurrences (all)	11	11	20
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	7 / 95 (7.37%)	6 / 88 (6.82%)	7 / 87 (8.05%)
occurrences (all)	7	7	10
Dry mouth			
subjects affected / exposed	1 / 95 (1.05%)	0 / 88 (0.00%)	6 / 87 (6.90%)
occurrences (all)	1	0	6
Nausea			
subjects affected / exposed	12 / 95 (12.63%)	7 / 88 (7.95%)	11 / 87 (12.64%)
occurrences (all)	14	8	16
Vomiting			
subjects affected / exposed	10 / 95 (10.53%)	3 / 88 (3.41%)	7 / 87 (8.05%)
occurrences (all)	12	3	7
Psychiatric disorders			
Anxiety			
subjects affected / exposed	6 / 95 (6.32%)	2 / 88 (2.27%)	12 / 87 (13.79%)
occurrences (all)	7	3	18
Insomnia			
subjects affected / exposed	4 / 95 (4.21%)	2 / 88 (2.27%)	11 / 87 (12.64%)
occurrences (all)	4	3	12
Irritability			
subjects affected / exposed	7 / 95 (7.37%)	1 / 88 (1.14%)	1 / 87 (1.15%)
occurrences (all)	7	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 95 (3.16%)	5 / 88 (5.68%)	2 / 87 (2.30%)
occurrences (all)	3	6	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	18 / 95 (18.95%)	12 / 88 (13.64%)	8 / 87 (9.20%)
occurrences (all)	25	13	9
Urinary tract infection			
subjects affected / exposed	5 / 95 (5.26%)	3 / 88 (3.41%)	4 / 87 (4.60%)
occurrences (all)	6	4	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported