Clinical trial results:
A Phase 3, Multinational, Randomized, Placebo-controlled Study of ARRY-371797 (PF-07265803) in Patients with Symptomatic Dilated Cardiomyopathy Due to a Lamin A/C Gene Mutation (REALM-DCM)

Summary

EudraCT number	2017-004310-25
Trial protocol	GB NO BE ES NL IT DK
Global end of trial date	13 October 2022

Results information

Result version number	v1 (current)
This version publication date	19 October 2023
First version publication date	19 October 2023

Trial information

Trial identification

Sponsor protocol code	C4411002 (Array-797-301)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03439514
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., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 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	12 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of ARRY-371797 (PF-07265803) on functional capacity as measured by the 6-minute walk test (6MWT) compared to placebo in subjects with symptomatic dilated cardiomyopathy (DCM) due to a Lamin A/C protein (LMNA) gene mutation.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2018
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	Belgium: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 27
Worldwide total number of subjects	77
EEA total number of subjects	46

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)	66
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total

Pre-assignment

Screening details:

A total of 77 subjects with Lamin A/C protein (LMNA)-related dilated cardiomyopathy (DCM) in New York heart association (NYHA) functional Class II and III were enrolled in the study. All subjects enrolled received at least 1 dose of study intervention.

Period 1

Period 1 title	Double-Blind Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-07265803 (ARRY-371797)

Arm description:

Subjects were randomised to receive PF-07265803 400 mg (4*100 mg tablets) twice daily (BID).

Arm type	Experimental
Investigational medicinal product name	PF-07265803
Investigational medicinal product code	
Other name	ARRY-371797
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received 400 mg (4*100 mg) twice daily (BID).

Arm title	Placebo

Arm description:

Subjects were randomised to receive placebo matched to PF-07265803 BID.

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

Dosage and administration details:

Subjects received placebo matched to PF-07265803.

Number of subjects in period 1	PF-07265803 (ARRY-371797)	Placebo
Started	40	37
Completed	0	0
Not completed	40	37
Adverse event, serious fatal	1	2
Consent withdrawn by subject	4	2
Not specified	4	1
Study Termination by Sponsor	29	32
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	PF-07265803 (ARRY-371797)
Reporting group description:	
Subjects were randomised to receive PF-07265803 400 mg (4*100 mg tablets) twice daily (BID).	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomised to receive placebo matched to PF-07265803 BID.	

Reporting group values	PF-07265803 (ARRY-371797)	Placebo	Total
Number of subjects	40	37	77
Age Categorical Units: Subjects			
18-34 years	4	1	5
35-49 years	15	10	25
50-64 years	17	19	36
>= 65 years	4	7	11
Sex: Female, Male Units: Subjects			
Female	18	15	33
Male	22	22	44
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	38	36	74
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	4	7
Not Hispanic or Latino	37	33	70
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	PF-07265803 (ARRY-371797)
Reporting group description:	
Subjects were randomised to receive PF-07265803 400 mg (4*100 mg tablets) twice daily (BID).	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomised to receive placebo matched to PF-07265803 BID.	

Primary: Change From Baseline in Six-Minute Walk Test (6 MWT) at Week 24

End point title	Change From Baseline in Six-Minute Walk Test (6 MWT) at Week 24

End point description:

The 6 MWT was an assessment where the distance that a subject could walk on a flat and hard surface in 6 minutes was measured. Subjects were asked to perform the test at a pace that was comfortable to them, with as many breaks as they needed, and under supervision of a qualified professional. Study discontinuation & death were incorporated into endpoint definition through ranking in hypothesis testing of treatment difference. Missing data resulting from study discontinuation were imputed using control-based multiple imputation method to estimate treatment effect. Efficacy analysis set (EAS): functional Class II/III randomised subjects. 'Number of Subjects Analyzed' : subjects evaluable for endpoint & contributed data to table but may not have evaluable data for every row. Five subjects (ARRY-371797 [n=3], placebo [n=2]) discontinued study before week 24 due to sponsor’s decision to terminate & were excluded from primary analysis. “n”: subjects evaluable for each specified rows.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	35		
Units: Meter				
median (inter-quartile range (Q1-Q3))				
Baseline median (n=35,33)	402.500 (348.195 to 444.000)	393.935 (360.000 to 425.500)		
Week 24 median (n=35,33)	420.234 (358.902 to 459.117)	393.455 (347.409 to 450.826)		
Week 24 median change from baseline (n=35,33)	20.996 (-22.757 to 51.477)	2.679 (-11.530 to 33.698)		

Statistical analyses

Statistical analysis title	PF-07265803 vs Placebo
Comparison groups	PF-07265803 (ARRY-371797) v Placebo

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.818 [1]
Method	Van Elteren test
Parameter estimate	Median difference (net)
Point estimate	4.936
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.246
upper limit	34.118

Notes:

[1] - Two-sided p-value

Secondary: Change From Baseline in 6 MWT at Weeks 4 and 12

End point title	Change From Baseline in 6 MWT at Weeks 4 and 12

End point description:

The 6 MWT was an assessment where the distance that a subject could walk on a flat and hard surface in 6 minutes was measured. Subjects were asked to perform the test at a pace that was comfortable to them, with as many breaks as they needed, and under supervision of a qualified professional. EAS included all NYHA functional Class II or III randomised subjects. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. n= number of subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Meter				
median (full range (min-max))				
Change at Week 4 (n=35, 32)	15.40 (-72.0 to 71.8)	-2.60 (-85.0 to 34.5)		
Change at Week 12 (n=33, 33)	21.47 (-70.2 to 69.3)	10.00 (-100.9 to 89.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Physical Limitation (PL) and Total Symptom Score (TSS) Domain Scores at Weeks 12 and 24

End point title	Change From Baseline in Kansas City Cardiomyopathy Questionnaire (KCCQ) Physical Limitation (PL) and Total Symptom Score (TSS) Domain Scores at Weeks 12 and 24

End point description:

The KCCQ measured the effects of symptoms, functional (physical) limitations, and psychological distress on an individual's health-related quality of life. It contains 23 items, which assessed the ability to perform activities of daily living, frequency and severity of symptoms, the impact of these symptoms, and health-related quality of life. PL was a single questionnaire with score range of 0 to 100, where higher scores reflected better physical functioning status. TSS included frequency and severity of symptoms, and the impact of these symptoms. TSS scores were transformed to a range of 0 to 100, where higher scores reflected better health status. EAS included all NYHA functional Class II or III randomised subjects. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. n= number of subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 12 Physical Limitation (n=33, 32)	4.48 (± 11.373)	-1.17 (± 15.326)		
Week 24 Physical Limitation (n=28, 31)	2.98 (± 17.510)	1.21 (± 14.104)		
Week 12 Total Symptom Score (n=33, 32)	3.66 (± 12.487)	1.04 (± 16.491)		
Week 24 Total Symptom Score (n=28, 31)	4.02 (± 19.171)	-0.94 (± 14.981)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Improvement From Baseline in Patient Global Impression of Severity (PGI-S) Score at Weeks 12 and 24

End point title	Number of Subjects With Improvement From Baseline in Patient Global Impression of Severity (PGI-S) Score at Weeks 12 and 24

End point description:

PGI-S is a global index that rate the severity of the disease using a 5-point scale. In this endpoint, the number of subjects with improvements in PGI-S the severity of their heart failure (HF) symptoms and in the severity of their PL were reported. Measured by the scale of: none, mild, moderate, severe or very severe (listed from better to worse). EAS included all NYHA functional Class II or III randomised subjects. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. n= number of subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Week 12, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Week 12: HF symptoms|None (n=33, 32)	4	5		
Week 24: HF symptoms|None (n=28, 31)	4	6		
Week 12: Physical limitation|None (n=33, 32)	6	7		
Week 24: Physical limitation|None (n=28, 31)	6	6		
Week 12: HF symptoms|Mild (n=33, 32)	16	14		
Week 24: HF symptoms|Mild (n=28, 31)	11	10		
Week 12: Physical limitation|Mild (n=33, 32)	11	5		
Week 24: Physical limitation|Mild (n=28, 31)	5	7		
Week 12: HF symptoms|Moderate (n=33, 32)	8	10		
Week 24: HF symptoms|Moderate (n=28, 31)	10	12		
Week 12: Physical limitation|Moderate (n=33, 32)	12	15		
Week 24: Physical limitation|Moderate (n=28, 31)	13	15		
Week 12: HF symptoms|Severe (n=33, 32)	4	2		
Week 24: HF symptoms|Severe (n=28, 31)	3	3		
Week 12: Physical limitation|Severe (n=33, 32)	3	4		
Week 24: Physical limitation|Severe (n=28, 31)	4	3		
Week 12: HF symptoms|Very Severe (n=33, 32)	1	1		
Week 24: HF symptoms|Very Severe (n=28, 31)	0	0		
Week 12:Physical limitation|Very Severe (n=33, 32)	1	1		
Week 24:Physical limitation|Very Severe (n=28, 31)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Improvement From Baseline in Patient Global Impression of Change (PGI-C) Score at Weeks 12 and 24

End point title	Number of Subjects With Improvement From Baseline in Patient Global Impression of Change (PGI-C) Score at Weeks

	12 and 24

End point description:

PGI-C is a global index that rate the severity of the disease using a 7-point scale. In this endpoint, the number subjects with improvements in their heart failure symptoms (HFS) and "in their physical activity limitations (PL)?", were reported. Measured by the scale of: very much better, moderately better, a little better, no change, a little worse, moderately worse, very much worse (listed from better to worse). EAS included all NYHA functional Class II or III randomised subjects. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. n= number of subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Week 12, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Week 12: Change in HFS|Very Much Better (n=33,32)	0	2		
Week 24: Change in HFS|Very Much Better (n=28,29)	1	1		
Week 12: Change in PL|Very Much Better (n=33,32)	0	1		
Week 24: Change in PL|Very Much Better (n=28,29)	1	1		
Week 12: Change in HFS|Moderately Better (n=33,32)	3	1		
Week 24: Change in HFS|Moderately Better (n=28,29)	3	2		
Week 12: Change in PL|Moderately Better (n=33,32)	3	2		
Week 24: Change in PL|Moderately Better (n=28,29)	3	0		
Week 12: Change in HFS|A Little Better (n=33,32)	7	9		
Week 24: Change in HFS|A Little Better (n=28,29)	7	6		
Week 12: Change in PL|A Little Better (n=33,32)	3	5		
Week 24: Change in PL|A Little Better (n=28,29)	3	4		
Week 12: Change in HFS|No Change (n=33,32)	18	17		
Week 24: Change in HFS|No Change (n=28,29)	16	16		
Week 12: Change in PL|No Change (n=33,32)	24	21		
Week 24: Change in PL|No Change (n=28,29)	19	20		
Week 12: Change in HFS|A Little Worse (n=33,32)	3	1		
Week 24: Change in HFS|A Little Worse (n=28,29)	0	2		
Week 12: Change in PL|A Little Worse (n=33,32)	0	1		

Week 24: Change in PL|A Little Worse (n=28,29)	1	3		
Week 12: Change in HFS|Moderately Worse (n=33,32)	1	0		
Week 24: Change in HFS|Moderately Worse (n=28,29)	1	1		
Week 12: Change in PL|Moderately Worse (n=33,32)	3	1		
Week 24: Change in PL|Moderately Worse (n=28,29)	1	1		
Week 12: Change in HFS|Very Much Worse (n=33,32)	1	2		
Week 24: Change in HFS|Very Much Worse (n=28,29)	0	1		
Week 12: Change in PL|Very Much Worse (n=33,32)	0	1		
Week 24: Change in PL|Very Much Worse (n=28,29)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Composite Time to First Occurrence of All-Cause Mortality or Worsening Heart Failure (WHF)

End point title	Composite Time to First Occurrence of All-Cause Mortality or Worsening Heart Failure (WHF)

End point description:

Defined as the time from randomisation to the first occurrence of any event of death due to any cause, or worsening heart failure (HF-related hospitalisation or HF-related urgent care visit). Kaplan-Meier method and cox regression model were used for analysis. The safety analysis set (SAS) included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class. Number of events analysed (PF-07265803: 3, Placebo: 7). Here "99999" suggests that data could not be evaluated as there were less subjects with events.

End point type	Secondary

End point timeframe:

Maximum up to 212.28 weeks (maximum exposure was 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Weeks				
median (confidence interval 95%)	99999 (-99999 to 99999)	99999 (-99999 to 99999)		

Statistical analyses

Statistical analysis title	PF-07265803 (ARRY-371797) vs Placebo
Comparison groups	PF-07265803 (ARRY-371797) v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2257
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	1.39

Secondary: Change From Baseline in N-Terminal Pro-Brain Natriuretic Peptide (NTproBNP) at Weeks 4, 12, and 24

End point title	Change From Baseline in N-Terminal Pro-Brain Natriuretic Peptide (NTproBNP) at Weeks 4, 12, and 24

End point description:

NT pro-BNP is a cardiac biomarker that is released in the blood in response to changes in the pressure inside of the heart. Levels go up when heart failure develops or gets worse, and levels go down when heart failure is stable or improves. This biomarker helps to measure the changes in the severity of heart failure over time in response to therapy. EAS included all NYHA functional Class II or III randomised subjects. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. n= signifies number of subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: picomoles per liter				
arithmetic mean (standard deviation)				
Change at Week 4 (n=33,33)	-43.89 (± 65.465)	-3.07 (± 62.745)		
Change at Week 12 (n=31,32)	-36.40 (± 69.228)	-0.70 (± 54.870)		
Change at Week 24 (n=23,28)	5.00 (± 236.643)	24.37 (± 134.225)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as time from randomisation to death due to any cause. Subjects who did not have a death date were censored for OS at their last contact date. Kaplan-Meier method and cox regression model were used for analysis. The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class. Number of events analysed (PF-07265803: 3, Placebo: 3). Here "99999" suggests that data could not be evaluated as there were less subjects with events.

End point type	Secondary

End point timeframe:

From randomisation up to death due to any cause or censored date, maximum up to 212.28 weeks (maximum exposure was of 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Weeks				
median (confidence interval 95%)	99999 (-99999 to 99999)	99999 (-99999 to 99999)		

Statistical analyses

Statistical analysis title	PF-07265803 (ARRY-371797) vs Placebo
Comparison groups	PF-07265803 (ARRY-371797) v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.837
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	4.63

Secondary: Number of Subjects With Treatment Emergent Adverse Events (AEs) and by Severity

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs) and by Severity

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without

regard to possibility of causal relationship. Treatment-emergent AEs were events that occurred between first dose of study drug and up to 30 days after last dose. 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 hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both SAEs and all Non-SAEs. Grade >=3 AEs meant severe AEs. The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class.

End point type	Secondary

End point timeframe:

Maximum up to 212.28 weeks (maximum exposure was of 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Subjects with TEAEs	35	34		
Subjects with serious TEAEs	10	21		
Subjects with severe (Grades >=3) TEAEs	16	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Test Abnormalities

End point title	Number of Subjects With Laboratory Test Abnormalities

End point description:

Following parameters were analysed for laboratory examination: hematology (eosinophils, erythrocytes mean corpuscular hemoglobin/mean corpuscular volume [MCH/MCV], hemoglobin [Hb], hematocrit [HCT], granulocytes, leukocytes, lymphocytes, monocytes, platelets, neutrophils, nucleated erythrocytes); blood chemistry (alanine aminotransferase [ALT], albumin, alkaline phosphatase [ALP], aspartate aminotransferase [AST], bicarbonate, bilirubin, blood urea nitrogen, C-reactive protein, calcium, chloride, creatinine [Cr], creatine kinase [CK], epidermal growth factor receptor [EGFR], follicle stimulating hormone [FSH], gamma glutamyl transferase [GGT], glucose, magnesium, N-Terminal ProB-type natriuretic peptide [NT-proBNP], phosphate, potassium, protein, sodium, potassium, thyrotropin, troponin I, troponin T, urate). The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class.

End point type	Secondary

End point timeframe:

Maximum up to 212.28 weeks (maximum exposure was of 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Eosinophils: High (>0.8) 10^9/L	1	0		
Eosinophils/Leukocytes: High (>7) %	1	1		
Erythrocyte MCH Concentration: Low (<310) g/L	30	29		
Erythrocyte MCH: Low (<27) pg	6	3		
Erythrocyte MCH: High (>34) pg	0	1		
Erythrocyte MCV: Low (Males <78, Females <82)	2	2		
Erythrocyte MCV: High (Males >100, Females >102)	10	15		
Erythrocytes:Low(Males:<4.63, Females:<3.7)10^12/L	14	16		
Erythrocyte:High(Males:>6.08, Females:>5.2)10^12/L	4	4		
Erythrocytes Distribution Width: High (>14.5) %	22	20		
HCT: Low(Males:<0.37, Females:<0.33) L/L	1	3		
HCT: High(Males:>0.51, Females:>0.47) L/L	12	15		
Hb: Low (Males: < 125; Females: <110) g/L	7	5		
Hb: High (Males: > 170; Females: > 155) g/L	5	4		
Immature Granulocytes: High (> 0.07) 10^9/L	9	7		
Immature Granulocytes/Leukocytes: High (> 1) %	6	6		
Leukocytes: Low (< 3.7) 10^9/L	1	0		
Leukocytes: High (> 11) 10^9/L	9	8		
Lymphocytes: Low (< 0.9) 10^9/L	3	4		
Lymphocytes: Low (> 3.6) 10^9/L	4	2		
Lymphocytes/Leukocytes: Low (< 12) %	3	3		
Lymphocytes/Leukocytes: High (> 46) %	2	1		
Mean Platelet Volume: Low (< 9.6) fL	5	0		
Mean Platelet Volume: High (> 13.8) fL	3	3		
Monocytes: High (> 1.2) 10^9/L	1	1		
Monocytes/Leukocytes: High (>11) %	11	10		
Neutrophils: Low (< 1.7) 10^9/L	1	1		
Neutrophils: High (> 7.9) 10^9/L	8	5		
Neutrophils/Leukocytes: High (>71) %	16	17		
Nucleated Erythrocytes: High (>0.01) 10^9/L	6	1		
Nucleated Erythrocytes/Leukocytes: High (>0.2) %	6	1		
Platelets: Low (< 163) 10^9/L	13	11		
Platelets: High (> 375) 10^9/L	2	1		
ALT: Low (< 10) U/L	4	5		
ALT: High (Males: > 40; Females: > 33) U/L	18	17		
Albumin: Low (< 35) g/L	1	0		

ALP: Low (Males: < 43; Females: <30) U/L	3	5		
ALP: High (> 115) U/L	4	5		
AST: High (Males: > 43; Females: > 36) U/L	11	8		
Bicarbonate: Low (< 21) mmol/L	9	12		
Bicarbonate: High (> 33) mmol/L	0	1		
Bilirubin: High (> 18.8) mcmol/L	4	12		
Blood Urea Nitrogen: High (> 7.14) mmol/L	28	27		
C Reactive Protein: High (> 47.6) nmol/L	20	19		
Calcium: Low (< 2.12) mmol/L	0	1		
Calcium: High (> 2.62) mmol/L	0	1		
Chloride: Low (< 95) mmol/L	2	1		
CK: Low (< 24) U/L	0	2		
CK: High (Males: > 207; Females: > 169) U/L	20	12		
Creatinine: Low (< 62) mcmol/L	14	13		
Creatinine: High (> 124) mcmol/L	4	6		
Cr Clearance: Low (Males:<85; Females:<75) mL/min	9	8		
Cr Clearance: High(Males:>125; Females:>115)mL/min	16	14		
Direct Bilirubin: High (> 6.8) mcmol/L	4	8		
EGFR: Low (Males: < 60) mL/min/1.73m2	1	0		
FSH: High (Males: > 12.4; Females: > 21.5) IU/L	2	4		
GGT: Low (Males: < 10; Females: <5) U/L	1	0		
GGT: High (Males: > 49; Females: > 32) U/L	15	27		
Glucose: Low(Males<3.94, Females <3.33) mmol/L	4	4		
Glucose: High (Males >7.66, Females >6.38) mmol/L	10	10		
Magnesium: High (> 1.05) mmol/L	1	1		
NT-proBNP: High (> 14.63) pmol/L	40	37		
Phosphate: Low (< 0.81) mmol/L	6	6		
Phosphate: High (> 1.45) mmol/L	8	4		
Potassium: Low (< 3.5) mmol/L	1	0		
Potassium: High (> 5) mmol/L	7	16		
Protein: Low (< 60) g/L	2	3		
Protein: High (> 80) g/L	2	3		
Sodium: High (> 145) mmol/L	1	1		
Thyrotropin: Low (< 0.27) mIU/L	1	1		
Thyrotropin: High (> 4.2) mIU/L	5	5		
Troponin I: High (> 0.3) mcg/L	4	6		
Troponin T: High (> 14) ng/L	36	34		
Urate: Low (Males:<0.238; Females:<0.119) mmol/L	3	2		
Urate: High (Males:>0.476; Females:>0.357) mmol/L	9	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects According to Categorisation of Abnormal Vital Signs

End point title	Number of Subjects According to Categorisation of Abnormal Vital Signs

End point description:

Following vital sign parameters were assessed: diastolic blood pressure (BP), systolic BP, heart rate, and body weight. Vital sign abnormalities criteria included: a) systolic blood pressure (mmHg): decrease (change <= -20, or value <90) and increase (change >=20, or value >140); b) diastolic blood pressure (mmHg): decrease (change <= -15, or value <60) and increase (change >=15, or value >90); c) heart Rate (bpm) decrease: (change <= -15, or value <50) and increase (change >=15, or value >100); d) weight: (kg) decrease (Change <= -7%) and increase (Change > =7%). The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class. "n" =subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Maximum up to 212.28 weeks (maximum exposure was of 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Systolic BP (mmHg): Decrease (n=37,37)	22	17		
Systolic BP (mmHg): Increase (n=37,37)	6	14		
Diastolic BP (mmHg): Decrease (n=37,37)	28	22		
Diastolic BP (mmHg): Increase (n=37,37)	7	18		
Heart Rate (bpm): Decrease (n=37,37)	7	9		
Heart Rate (bpm): Increase (n=37,37)	15	10		
Weight (kg): Decrease (n=36,35)	10	7		
Weight (kg): Increase (n=36,35)	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects According to Categorisation of Electrocardiogram (ECG) Data

End point title	Number of Subjects According to Categorisation of Electrocardiogram (ECG) Data

End point description:

Following parameters were analysed: heart rate, QT interval, corrected QT (QTc) interval, Bazett's correction QT (QTcB) interval, and Fridericia's correction (QTcF) interval. Criteria for notable ECG values were as follows: QT interval (in millisecond [msec]) new (newly occurring post-baseline value) greater than (>) 450, 480, 500, increase from baseline >30, increase from baseline >60; corrected QT interval by Fredericia formula (QTcF) in msec new (newly occurring post-baseline value) > 450, 480, 500, increase from baseline >30, increase from baseline >60; corrected QT interval by Bazett's formula (QTcB) in msec new (newly occurring post-baseline value) > 450, 480, 500, increase from baseline >30, increase from baseline >60; heart rate in bpm new (newly occurring post-baseline value) <60 and >100. The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class. "n" =subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Maximum up to 212.28 weeks (maximum exposure was of 208 weeks)

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: Subjects				
QTcB (msec): New >450 (n=10, 6)	5	4		
QTcB (msec): New >480 (n=17, 15)	10	4		
QTcB (msec): New >500 (n=23, 18)	11	2		
QTcB (msec): Increase from baseline >30 (n=28, 26)	12	4		
QTcB (msec): Increase from baseline >60 (n=28, 26)	5	1		
QTcF (msec): New >450 (n=10,6)	7	2		
QTcF (msec): New >480 (n=18,17)	9	3		
QTcF (msec): New >500 (n=24,20)	8	4		
QTcF (msec): Increase from baseline >30 (n=28,26)	11	4		
QTcF (msec): Increase from baseline >60 (n=28,26)	3	0		
QT (msec): New >450 (n=9,10)	5	4		
QT (msec): New >480 (n=21,18)	11	1		
QT (msec): New >500 (n=24,22)	2	1		
QT (msec): Increase from baseline >30 (n=28,26)	8	3		
QT (msec): Increase from baseline >60 (n=28,26)	2	0		
Heart rate (bpm): New <60 (n=18,19)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With a new Clinically Significant Ventricular or Atrial Arrhythmias

End point title	Number of Subjects With a new Clinically Significant Ventricular

	or Atrial Arrhythmias

End point description:

Arrhythmia assessment: incidence of new and clinically significant ventricular or atrial arrhythmias was assessed by an implantable cardioverter defibrillator (ICD) or CRT defibrillator (CRT-D) applicable device interrogations. The SAS included all subjects who received at least 1 dose of study intervention regardless of NYHA functional class. "n" =subjects evaluable for specified rows of respective arms.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 24

End point values	PF-07265803 (ARRY-371797)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: Subjects				
Baseline: Atrial arrhythmia (n=29, 25)	0	0		
Week 12: Atrial arrhythmia (n=20, 20)	0	2		
Week 24: Atrial arrhythmia (n=14, 15)	0	0		
Baseline: Ventricular arrhythmia (n=24, 24)	0	0		
Week 12: Ventricular arrhythmia (n=18, 18)	0	3		
Week 24: Ventricular arrhythmia (n=14, 15)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day1) up to a maximum of 208 weeks

Adverse event reporting additional description:

Same event may appear as both non-SAE and a serious AE. However, what is presented are distinct events. An event may be categorised 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. All subjects who receive any of the study intervention.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects were randomised to receive placebo matched to PF-07265803 BID.

Reporting group title	PF-07265803 (ARRY-371797)

Reporting group description:

Subjects were randomised to receive PF-07265803 400 mg (4*100 mg tablets) twice daily (BID).

Serious adverse events	Placebo	PF-07265803 (ARRY-371797)	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 37 (56.76%)	10 / 40 (25.00%)	
number of deaths (all causes)	3	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal cavity cancer			
alternative assessment type:			

Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Ejection fraction decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Thoracic vertebral fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	2 / 37 (5.41%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 37 (2.70%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	5 / 37 (13.51%)	5 / 40 (12.50%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	3 / 37 (8.11%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			

subjects affected / exposed	2 / 37 (5.41%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	3 / 37 (8.11%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			

subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
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			
Urticaria			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Gouty arthritis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia bacterial			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 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-07265803 (ARRY-371797)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 37 (72.97%)	31 / 40 (77.50%)	
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 37 (5.41%)	3 / 40 (7.50%)	
occurrences (all)	2	3	
SARS-CoV-2 test positive			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 37 (18.92%)	11 / 40 (27.50%)	
occurrences (all)	7	14	
Vascular disorders			

Hypotension alternative assessment type: Systematic subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5	4 / 40 (10.00%) 4	
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 10	6 / 40 (15.00%) 7	
Angina pectoris subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	3 / 40 (7.50%) 3	
Cardiac failure acute subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	2 / 40 (5.00%) 2	
Atrial flutter subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 5	3 / 40 (7.50%) 4	
Ventricular tachycardia subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 12	7 / 40 (17.50%) 10	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	9 / 40 (22.50%) 13	
Headache subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 12	4 / 40 (10.00%) 6	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 6	4 / 40 (10.00%) 5	
Gastrointestinal disorders Stomatitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	5 / 40 (12.50%) 7	

Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 37 (8.11%)	2 / 40 (5.00%)	
occurrences (all)	4	4	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 37 (13.51%)	7 / 40 (17.50%)	
occurrences (all)	7	9	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 37 (10.81%)	12 / 40 (30.00%)	
occurrences (all)	7	19	
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 37 (10.81%)	3 / 40 (7.50%)	
occurrences (all)	6	3	
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 37 (8.11%)	2 / 40 (5.00%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	6 / 37 (16.22%)	1 / 40 (2.50%)	
occurrences (all)	8	2	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 37 (2.70%)	5 / 40 (12.50%)	
occurrences (all)	1	7	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 37 (5.41%)	3 / 40 (7.50%)	
occurrences (all)	2	3	

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