



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

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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|
| End point title | Change From Baseline in Six-Minute Walk Test (6 MWT) at Week 24 |
| End point description: | |
| <p>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.</p> | |
| 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

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| 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.

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|----------------|-----------|
| 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 |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

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

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|-----------------|----------------------------------------------------------------------------------------------------|
| 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: 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: Overall Survival (OS)

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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| 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 $\leq -7\%$) and increase (Change $\geq 7\%$). 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 |
|-----------------|------------------------------------------------------------------|

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