



Clinical trial results:

A Phase 2A, Randomized, double blind, parallel group, placebo controlled, multi center study to assess the efficacy and safety profile of PF-06651600 in subjects with moderate to severe active rheumatoid arthritis with an inadequate response to methotrexate

Summary

EudraCT number	2016-002862-30
Trial protocol	HU CZ SK BG DE PL
Global end of trial date	12 December 2017

Results information

Result version number	v1 (current)
This version publication date	22 November 2018
First version publication date	22 November 2018

Trial information

Trial identification

Sponsor protocol code	B7981006
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 110017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of PF-06651600 at 8 weeks in subjects with moderate to severe active rheumatoid arthritis.

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 Harmonization (ICH) Good Clinical Practice (GCP)

Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 15
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Georgia: 20
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Serbia: 14
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	70
EEA total number of subjects	31

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)	55
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Seventy subjects were enrolled at different centers in 8 countries between 2 February 2017 and 12 December 2017.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06651600

Arm description:

Subjects received 200 milligram (mg) of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

Arm type	Experimental
Investigational medicinal product name	PF-06651600
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 200 mg of PF-06651600 tablet once daily.

Arm title	Placebo
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Arm description:

Subjects received placebo matched to 200 mg of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

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

Dosage and administration details:

Subjects received placebo matched to PF-06651600 200 mg tablet once daily.

Number of subjects in period 1	PF-06651600	Placebo
Started	42	28
Completed	37	22
Not completed	5	6
Consent withdrawn by subject	2	6
Adverse event, non-fatal	3	-

Baseline characteristics

Reporting groups

Reporting group title	PF-06651600
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Reporting group description:

Subjects received 200 milligram (mg) of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo matched to 200 mg of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

Reporting group values	PF-06651600	Placebo	Total
Number of subjects	42	28	70
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	33	22	55
From 65-84 years	9	6	15
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	55.4	54.2	-
standard deviation	± 11.72	± 11.78	-
Sex: Female, Male			
Units: Subjects			
Female	33	24	57
Male	9	4	13
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	41	28	69
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	2	3
Not Hispanic or Latino	41	26	67
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	PF-06651600
Reporting group description: Subjects received 200 milligram (mg) of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.	
Reporting group title	Placebo
Reporting group description: Subjects received placebo matched to 200 mg of PF-06651600 tablet once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.	

Primary: Change From Baseline in Simple Disease Activity Index (SDAI) Score at Week 8

End point title	Change From Baseline in Simple Disease Activity Index (SDAI) Score at Week 8
End point description: The SDAI is the numerical sum of five outcome parameters: tender joint count (TJC) and swollen joint count (SJC) based on a 28-joint assessment, subject global assessment (PtGA) and physician global assessment (PGA) assessed on a visual analog scale (VAS) ranging from 0 to 10 centimeter (cm), where higher scores=greater affection due to disease activity, and C-reactive protein (CRP) measured in terms of milligram per deciliter (mg/dL). SDAI total score= 0 to 86. SDAI greater than or equal to (\leq) 3.3 indicates disease remission, greater than ($>$) 3.4 to 11 = low disease activity, >11 to 26 = moderate disease activity, and >26 = high disease activity. Intent to treat (ITT) analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n=number of subjects evaluable at specified time points only.	
End point type	Primary
End point timeframe: Baseline, Week 8	

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	45.15 (\pm 13.164)	44.85 (\pm 13.976)		
Change at Week 8 (n =39, 24)	-26.11 (\pm 14.834)	-17.38 (\pm 18.176)		

Statistical analyses

Statistical analysis title	PF-06651600 vs Placebo
Comparison groups	PF-06651600 v Placebo

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-9.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.75
upper limit	-3.79

Secondary: Number of Subjects With Vital Signs Abnormalities

End point title	Number of Subjects With Vital Signs Abnormalities
End point description:	
Criteria: sitting pulse rate less than (<) 40 beats per minute (bpm) or >120 bpm; sitting systolic blood pressure (SBP) \geq 30 millimeters of mercury (mmHg) change from baseline in same posture or <90 mmHg; diastolic blood pressure (DBP) \geq 20 mmHg change from baseline in same posture or <50 mmHg. Only those categories in which at least one subject had abnormality, were reported in this endpoint. Safety analysis set included all subjects who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe:	
Baseline up to Week 12	

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: subjects				
Sitting DBP \geq 20 mmHg increase from baseline	3	0		
Sitting DBP \geq 20 mmHg decrease from baseline	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities
End point description:	
Hemoglobin(Hb);hematocrit;RBC count:<0.8*lower limit of normal (LLN),mean corpuscular volume;mean corpuscular Hb concentration:<0.9*LLN or>1.1*upper limit of normal (ULN), platelet:<0.5*LLN or >1.75*ULN,reticulocytes <0.5*LLN or >1.5*ULN,leukocytes <0.6*LLN or >1.5*ULN,lymphocyte;neutrophil: <0.8*LLN or >1.2*ULN,basophil;eosinophil; monocyte:>1.2*ULN,partial thromboplastin time,prothrombin time>1.1*ULN,bilirubin>1.5*ULN, aspartate aminotransferase; alanine	

aminotransferase;alkaline phosphatase:>3.0*ULN,protein;albumin;LDL, HDL cholestrol:<0.8*LLN or >1.2*ULN;urea nitrogen;creatinine: >1.3*ULN, urate >1.2*ULN, sodium<0.95*LLN or >1.05*ULN, potassium; chloride;calcium; bicarbonate:<0.9*LLN or >1.1*ULN,glucose <0.6*LLN or >1.5*ULN, creatine kinase: >2.0*ULN;urine pH <4.5 or >8,urine glucose or ketones>=1,urine protein;urineHb>=1,urobilinogen;bilirubin;nitrite;leukocyte esterase >=1,urine erythrocytes, leukocytes>=20,hyaline cast>1,bacteria>20.Safety set.

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: subjects	42	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)
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End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to Week 12 that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline up to Week 12

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: subjects				
AEs	20	5		
SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simple Disease Activity Index (SDAI) Score at Week 1, 2, 4 and 6

End point title	Change From Baseline in Simple Disease Activity Index (SDAI) Score at Week 1, 2, 4 and 6
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End point description:

The SDAI is the numerical sum of five outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on a VAS scale ranging from 0 to 10 cm, where higher scores=greater affection due to disease activity, and CRP measured in terms of mg/dL. SDAI total score= 0 to 86. SDAI \leq 3.3 indicates disease remission, $>$ 3.4 to 11 = low disease activity, $>$ 11 to 26 = moderate disease activity, and $>$ 26 = high disease activity. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, and 6

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 1 (n =40, 28)	-4.59 (\pm 9.409)	-4.52 (\pm 7.025)		
Change at Week 2 (n =42, 27)	-12.82 (\pm 10.969)	-8.05 (\pm 9.402)		
Change at Week 4 (n =41, 26)	-17.79 (\pm 12.804)	-12.55 (\pm 13.462)		
Change at Week 6 (n =40, 26)	-22.79 (\pm 14.007)	-15.62 (\pm 14.231)		

Statistical analyses

No statistical analyses for this end point

Secondary: Remission Rate Based on Simple Disease Activity Index Score

End point title	Remission Rate Based on Simple Disease Activity Index Score
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End point description:

Remission rate was defined as percentage of subjects with disease remission. The SDAI is the numerical sum of five outcome parameters: TJC and SJC based on a 28-joint assessment, PtGA and PGA assessed on 0-10 cm VAS; higher scores=greater affection due to disease activity, and CRP (mg/dL). SDAI total score= 0-86. SDAI \leq 3.3 indicates disease remission, $>$ 3.4 to 11 = low disease activity, $>$ 11 to 26 = moderate disease activity, and $>$ 26 = high disease activity. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo).

End point type	Secondary
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End point timeframe:

Week 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percentage of subjects				
number (not applicable)				
Week 4	4.8	0.0		
Week 6	4.8	0.0		
Week 8	7.1	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Remission Rate Based on Disease Activity score (DAS28-4[ESR])

End point title	Remission Rate Based on Disease Activity score (DAS28-4[ESR])
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End point description:

Remission rate was defined as the percentage of subjects with disease remission. DAS28 was calculated from the number of SJC and TJC using the 28 joints count, the erythrocyte sedimentation rate (ESR) (millimeter per hour [mm/hour]) and subject's global assessment (PGA) of disease activity (subject rated arthritis activity assessment with transformed scores ranging 0 to 10; higher scores indicated greater affectation due to disease activity). DAS28 ≤ 3.2 = low disease activity, DAS28 > 3.2 to 5.1 = moderate to high disease activity. Subjects who had DAS28 ≤ 3.2 were considered in remission or LDA state. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo).

End point type	Secondary
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End point timeframe:

Week 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percentage of subjects				
number (not applicable)				
Week 4: DAS28-4(ESR)	4.8	0.0		
Week 6: DAS28-4(ESR)	4.8	0.0		
Week 8: DAS28-4(ESR)	7.1	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Remission Rate Based on Disease Activity score (DAS28-3 [ESR])

End point title	Remission Rate Based on Disease Activity score (DAS28-3 [ESR])
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End point description:

Remission rate was defined as the percentage of subjects with disease remission. DAS28 is measure of disease activity in subjects with rheumatoid arthritis. DAS28-3 (ESR) was calculated from SJC and TJC using 28 joints count, and ESR (millimeters per hour [mm/hour]). Total score range: 0-9.4, higher score=more disease activity. DAS28-3 (ESR) ≤ 3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-3 (ESR) <2.6 = remission. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo).

End point type	Secondary
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End point timeframe:

Week 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percentage of subjects				
number (not applicable)				
Week 4	4.8	0.0		
Week 6	2.4	0.0		
Week 8	7.1	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Remission Rate Based on Disease Activity score (DAS28-4 [CRP])

End point title	Remission Rate Based on Disease Activity score (DAS28-4 [CRP])
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End point description:

Remission rate was defined as the percentage of subjects with disease remission. DAS28 is measure of disease activity in subjects with rheumatoid arthritis. DAS28-4 (CRP): calculated from SJC, TJC, CRP (mg/L) and PGA (subject rated disease activity on VAS from 0 to 100 mm; high score=worse health). Total score range of DAS28-4 (CRP): 0 to 9.4(0=no activity; 9.4=extreme disease activity), higher score=more disease activity. DAS28-4(CRP) <2.6 =remission, <3.2 =low disease activity, ≥ 3.2 -5.1=moderate disease activity and >5.1 =high disease activity. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo).

End point type	Secondary
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End point timeframe:

Week 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percentage of subjects				
number (not applicable)				
Week 4	9.5	0.0		
Week 6	9.5	3.6		
Week 8	9.5	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Remission Rate Based on Disease Activity score (DAS28-3 [CRP])

End point title	Remission Rate Based on Disease Activity score (DAS28-3 [CRP])
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End point description:

Remission rate was defined as the percentage of subjects with disease remission. DAS28 is measure of disease activity in subjects with rheumatoid arthritis. DAS28-3 (CRP) was calculated from the SJC and TJC using the 28 joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-3 (CRP) ≤ 3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-3 (CRP) <2.6 = remission. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo).

End point type	Secondary
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End point timeframe:

Week 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percentage of subjects				
number (not applicable)				
Week 4	9.5	0.0		
Week 6	7.1	3.6		
Week 8	9.5	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score Based on 28-Joints Count and Erythrocyte Sedimentation Rate (3 Variables) (DAS28-3 [ESR]) at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Disease Activity Score Based on 28-Joints Count and Erythrocyte Sedimentation Rate (3 Variables)
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End point description:

DAS28 is measure of disease activity in subjects. DAS28-3 (ESR) was calculated from SJC and TJC using 28 joints count, and ESR (mm/hour). Total score range: 0-9.4, higher score=more disease activity. DAS28-4 (ESR) ≤ 3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-4 (ESR) <2.6 = remission. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	6.49 (\pm 0.762)	6.37 (\pm 0.815)		
Change at Week 1 (n =40, 28)	-0.19 (\pm 0.604)	-0.26 (\pm 0.434)		
Change at Week 2 (n =42, 27)	-0.67 (\pm 0.602)	-0.46 (\pm 0.531)		
Change at Week 4 (n =41, 26)	-1.16 (\pm 1.125)	-0.78 (\pm 0.905)		
Change at Week 6 (n =40, 25)	-1.54 (\pm 1.123)	-1.07 (\pm 0.989)		
Change at Week 8 (n =39, 24)	-1.85 (\pm 1.161)	-1.07 (\pm 1.214)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score Based on 28-Joints Count and Erythrocyte Sedimentation Rate (4 Variables) (DAS28-4 [ESR]) at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Disease Activity Score Based on 28-Joints Count and Erythrocyte Sedimentation Rate (4 Variables) (DAS28-4 [ESR]) at Week 1, 2, 4, 6 and 8
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End point description:

DAS28 is measure of disease activity in subjects. DAS28-4 (ESR) was calculated from SJC and TJC using 28 joints count, ESR (mm/hour) and PtGA of disease activity (subject rated arthritis activity assessment). Total score range: 0-9.4, higher score=more disease activity. DAS28-4 (ESR) ≤ 3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-4 (ESR) <2.6 = remission. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	6.82 (± 0.815)	6.72 (± 0.880)		
Change at Week 1 (n =40, 28)	-0.27 (± 0.553)	-0.27 (± 0.477)		
Change at Week 2 (n =42, 27)	-0.83 (± 0.695)	-0.47 (± 0.551)		
Change at Week 4 (n =41, 26)	-1.36 (± 1.173)	-0.89 (± 0.951)		
Change at Week 6 (n =40, 25)	-1.81 (± 1.179)	-1.18 (± 1.050)		
Change at Week 8 (n =39, 24)	-2.14 (± 1.269)	-1.22 (± 1.448)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score Based on 28-Joints Count and C-Reactive Protein (3 Variables) (DAS28-3 [CRP]) at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Disease Activity Score Based on 28-Joints Count and C-Reactive Protein (3 Variables) (DAS28-3 [CRP]) at Week 1, 2, 4, 6 and 8
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End point description:

DAS28 is measure of disease activity in subjects. DAS28-3 (CRP) was calculated from the SJC and TJC using the 28 joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-3 (CRP) ≤ 3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-3 (CRP) <2.6 = remission. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	5.76 (± 0.824)	5.61 (± 0.894)		
Change at Week 1 (n =40, 28)	-0.35 (± 0.741)	-0.20 (± 0.456)		

Change at Week 2 (n =42, 27)	-0.86 (± 0.782)	-0.47 (± 0.585)		
Change at Week 4 (n =41, 26)	-1.33 (± 1.219)	-0.72 (± 1.005)		
Change at Week 6 (n =40, 26)	-1.53 (± 1.286)	-1.01 (± 0.993)		
Change at Week 8 (n =39, 24)	-1.79 (± 1.265)	-1.03 (± 1.146)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score Based on 28-Joints Count and C-Reactive Protein (4 Variables) (DAS28-4 [CRP]) at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Disease Activity Score Based on 28-Joints Count and C-Reactive Protein (4 Variables) (DAS28-4 [CRP]) at Week 1, 2, 4, 6 and 8
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End point description:

DAS28 is measure of disease activity in subjects. DAS28-4 (CRP): calculated from SJC, TJC, CRP(mg/L) and PGA (subject rated disease activity on VAS from 0 to 100 mm; high score=worse health). Total score range of DAS28-4 (CRP): 0 to 9.4(0=no activity; 9.4=extreme disease activity), higher score=more disease activity. DAS28-4(CRP) <2.6=remission, <3.2=low disease activity, >=3.2-5.1=moderate disease activity and >5.1=high disease activity. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	6.11 (± 0.850)	5.98 (± 0.926)		
Change at Week 1 (n =40, 28)	-0.41 (± 0.685)	-0.21 (± 0.473)		
Change at Week 2 (n =42, 27)	-0.99 (± 0.823)	-0.47 (± 0.574)		
Change at Week 4 (n =41, 26)	-1.49 (± 1.222)	-0.82 (± 1.013)		
Change at Week 6 (n =40, 26)	-1.78 (± 1.304)	-1.09 (± 1.057)		
Change at Week 8 (n =39, 24)	-2.06 (± 1.321)	-1.16 (± 1.367)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) Concentration at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in High Sensitivity C-Reactive Protein (hsCRP) Concentration at Week 1, 2, 4, 6 and 8
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End point description:

ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: milligram per deciliter				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	2.00 (± 1.816)	1.68 (± 2.853)		
Change at Week 1 (n =40, 28)	-0.20 (± 2.672)	0.60 (± 2.263)		
Change at Week 2 (n =42, 27)	-0.62 (± 2.090)	-0.04 (± 0.966)		
Change at Week 4 (n =41, 26)	-0.93 (± 1.591)	0.00 (± 1.335)		
Change at Week 6 (n =40, 26)	-0.42 (± 2.376)	-0.23 (± 1.327)		
Change at Week 8 (n =39, 24)	-0.89 (± 2.142)	-0.04 (± 2.220)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Tender Joint count and Swollen Joint count at Week 1, 2, 4, 6 and 8

End point title	Change from Baseline in the Tender Joint count and Swollen Joint count at Week 1, 2, 4, 6 and 8
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End point description:

Tender joint count was an assessment of 68 joints (upper body, upper extremity, and lower extremity). Each joint's response to pressure/motion was assessed as: Present or Absent. Swollen joint count was an assessment of 66 joints (upper body, upper extremity, and lower extremity). Each joint was assessed for swelling as: Present or Absent. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: joints				
arithmetic mean (standard deviation)				
Baseline: Tender joint count (n =42, 28)	16.74 (± 6.765)	16.75 (± 6.681)		
Baseline: Swollen joint count (n =42, 28)	12.95 (± 5.396)	12.11 (± 6.160)		
Change at Week 1: Tender joint count (n =41, 28)	-1.54 (± 4.915)	-1.96 (± 2.701)		
Change at Week 1: Swollen joint count (n =41, 28)	-1.49 (± 4.439)	-2.46 (± 3.501)		
Change at Week 2: Tender joint count (n =42, 27)	-4.40 (± 5.522)	-2.56 (± 5.213)		
Change at Week 2: Swollen joint count (n =42, 27)	-4.71 (± 4.430)	-4.11 (± 4.619)		
Change at Week 4: Tender joint count (n =41, 26)	-6.76 (± 6.818)	-4.96 (± 7.750)		
Change at Week 4: Swollen joint count (n =41, 26)	-5.95 (± 4.950)	-4.85 (± 4.961)		
Change at Week 6: Tender joint count (n =40, 26)	-8.75 (± 7.132)	-6.42 (± 6.652)		
Change at Week 6: Swollen joint count (n =40, 26)	-7.80 (± 5.743)	-5.85 (± 5.540)		
Change at Week 8: Tender joint count (n=39, 24)	-10.21 (± 7.259)	-6.83 (± 7.755)		
Change at Week 8: Swollen joint count (n =39, 24)	-8.59 (± 6.176)	-6.54 (± 6.324)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subject's Assessment of Arthritis Pain (PAAP), Subject's Global Assessment of Arthritis (PGA) and Physician's Global Assessment of Arthritis (PGAA) at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Subject's Assessment of Arthritis Pain (PAAP), Subject's Global Assessment of Arthritis (PGA) and Physician's Global Assessment of Arthritis (PGAA) at Week 1, 2, 4, 6 and 8
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End point description:

PAAP: Subjects assessed the severity of their arthritis pain by using a 100 mm VAS ranging from 0 (no pain) to 100 (most severe pain), which corresponded to the magnitude of their pain, where higher scores indicated more pain. PGA: Subjects were asked the following question, "Considering all the ways your arthritis affects you, how are you feeling today?" and their response was recorded on a 100 mm VAS ranging from 0 (very well) to 100 (very poor), where higher scores indicated worse health condition. PGAA: Subjects were assessed how their overall arthritis appears at the time of the visit. The evaluation was based on the subject's disease signs, functional capacity and physical examination, and was independent of the PAAP and PGA assessments. The physician's response was recorded using a 100 mm VAS ranging from 0 (very well) to 100 (very poor), where higher scores indicated more disease activity. ITT analysis set.n=number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: PAAP (n =42, 28)	66.64 (± 16.771)	71.75 (± 16.183)		
Baseline: PGA (n =42, 28)	68.43 (± 15.639)	69.00 (± 16.115)		
Baseline: PGAA (n =42, 28)	66.17 (± 14.228)	74.07 (± 12.844)		
Change at Week 1: PAAP (n =41, 28)	-4.95 (± 11.388)	-2.86 (± 14.847)		
Change at Week 1: PGA (n =41, 28)	-6.76 (± 11.128)	-1.93 (± 9.149)		
Change at Week 1: PGAA (n =41, 28)	-6.83 (± 8.947)	-4.96 (± 8.126)		
Change at Week 2: PAAP (n =42, 27)	-11.90 (± 18.061)	-6.04 (± 12.669)		
Change at Week 2: PGA (n =42, 27)	-14.74 (± 15.963)	-2.81 (± 9.931)		
Change at Week 2: PGAA (n =42, 27)	-16.07 (± 16.499)	-10.63 (± 12.500)		
Change at Week 4: PAAP (n =41, 26)	-19.88 (± 16.695)	-10.23 (± 25.513)		
Change at Week 4: PGA (n =41, 26)	-20.05 (± 13.746)	-12.12 (± 19.574)		
Change at Week 4: PGAA (n =41, 26)	-21.49 (± 16.715)	-17.96 (± 18.877)		
Change at Week 6: PAAP (n =40, 26)	-27.90 (± 20.061)	-12.35 (± 27.425)		
Change at Week 6: PGA (n =40, 26)	-27.83 (± 18.936)	-11.65 (± 21.630)		
Change at Week 6: PGAA (n =40, 26)	-30.45 (± 17.868)	-19.50 (± 22.963)		
Change at Week 8: PAAP (n =39, 24)	-32.92 (± 25.051)	-18.58 (± 34.152)		
Change at Week 8: PGA (n =39, 24)	-30.92 (± 21.279)	-15.88 (± 30.135)		
Change at Week 8: PGAA (n =39, 24)	-33.28 (± 18.725)	-23.75 (± 25.902)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire-Disability Index [HAQ-DI] at Week 1, 2, 4, 6 and 8

End point title	Change From Baseline in Health Assessment Questionnaire-
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End point description:

HAQ-DI assess degree of difficulty a subject experienced (during past week) in 8 domain of daily activities: dressing and grooming, arising, eating, walking, hygiene, reach, grip and other activities. Each item scored on a 4-point scale ranging from 0 to 3(0=no difficulty; 3=extreme difficulty). Overall score: average of the sum of domain scores/number of domains answered. Total possible score range (0=least difficulty; 3=extreme difficulty); high scores=more difficulty in performing daily living activities. ITT analysis set included all subjects who were randomized to the study and received at least one dose of the randomized investigational drug (PF-06651600 or placebo). Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Baseline, Week 1, 2, 4, 6 and 8

End point values	PF-06651600	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =42, 28)	1.79 (± 0.577)	1.69 (± 0.550)		
Change at Week 1 (n =41, 28)	-0.13 (± 0.391)	-0.04 (± 0.316)		
Change at Week 2 (n =42, 27)	-0.26 (± 0.430)	-0.15 (± 0.347)		
Change at Week 4 (n =41, 26)	-0.39 (± 0.414)	-0.19 (± 0.534)		
Change at Week 6 (n =40, 26)	-0.46 (± 0.527)	-0.23 (± 0.609)		
Change at Week 8 (n =39, 24)	-0.53 (± 0.583)	-0.32 (± 0.671)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 12

Adverse event reporting additional description:

Same event may appear as both an adverse event and serious adverse event. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	v20.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo matched to 200 mg of PF-06651600 tablets once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

Reporting group title	PF-06651600
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Reporting group description:

Subjects received 200 mg of PF-06651600 tablets once daily for a period of 8 weeks. Subjects were followed up to 4 weeks after last dose of investigational drug.

Serious adverse events	Placebo	PF-06651600	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 42 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	PF-06651600	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 28 (17.86%)	20 / 42 (47.62%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 42 (0.00%) 0	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Cytomegalovirus test positive subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Ligament sprain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	0 / 42 (0.00%) 0	
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 42 (7.14%) 3	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Glossitis			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Nausea subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Vomiting subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Dermatitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Pruritus subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	2 / 42 (4.76%) 2	
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Psychiatric disorders Suicidal ideation subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 42 (2.38%) 1	
Spinal pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 42 (0.00%) 0	

Synovitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Fungal skin infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Oral herpes			
subjects affected / exposed	0 / 28 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 42 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2016	To monitor for potential changes in hearing between baseline (between Visit 1 and Visit 2 [inclusive]) and at the end of the study (between Visit 7 and Visit 9 [inclusive]).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported