Clinical trial results:
A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, MULTICENTER, DOSE-RANGING STUDY TO EVALUATE THE EFFICACY AND SAFETY OF PF-04236921 IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Summary

EudraCT number	2011-000420-15
Trial protocol	DE HU
Global end of trial date	26 March 2014

Results information

Result version number	v1
This version publication date	08 March 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	B0151006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01405196
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., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, 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	01 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate and compare the efficacy of 3 dose levels of PF-04236921 to placebo in subjects with active SLE using the SLE Responder Index (SRI).

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 Conference on 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	16 December 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Argentina: 28
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Moldova, Republic of: 15
Country: Number of subjects enrolled	Peru: 4
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	United States: 92
Worldwide total number of subjects	183
EEA total number of subjects	32

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)	179
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study started on 8 November 2011 and completed on 26 March 2014. Subjects were enrolled from 11 countries (Argentina, Chile, Columbia, Germany, Hungary, Republic of Korea, Republic of Moldova, Peru, Poland, Romania and United states).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-04236921 10 milligram (10 mg)

Arm description:

Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

10 mg dose of PF-04236921 subcutaneously at Week 0, Week 8 and Week 16.

Arm title	PF-04236921 50 mg

Arm description:

Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

50 mg dose of PF-04236921 subcutaneously at Week 0, Week 8 and Week 16.

Arm title	PF-04236921 200 mg

Arm description:

Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.

Arm type	Experimental
Investigational medicinal product name	PF-04236921
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg dose of PF-04236921 subcutaneously at Week 0, Week 8 and Week 16.

Arm title	Placebo

Arm description:

Placebo matching to PF-04236921 administered subcutaneously in the anterolateral right and left thighs.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously in the anterolateral right and left thighs at Week 0, Week 8 and Week 16.

Number of subjects in period 1	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg
Started	45	47	46
Completed	34	35	23
Not completed	11	12	23
Consent withdrawn by subject	4	6	3
'Study Terminated by Sponsor '	-	-	9
Adverse Event	2	2	-
Unspecified	2	2	5
Lost to follow-up	2	2	3
Subject Died	1	-	3

Number of subjects in period 1	Placebo
Started	45
Completed	36
Not completed	9
Consent withdrawn by subject	6
'Study Terminated by Sponsor '	-
Adverse Event	2
Unspecified	-
Lost to follow-up	1
Subject Died	-

Baseline characteristics

Reporting groups	
Reporting group title	PF-04236921 10 milligram (10 mg)
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	PF-04236921 50 mg
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	PF-04236921 200 mg
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	Placebo
Reporting group description:	
Placebo matching to PF-04236921 administered subcutaneously in the anterolateral right and left thighs.	

Reporting group values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg
Number of subjects	45	47	46
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 39.9 ± 11.48	 38.3 ± 10.49	 41.3 ± 11.29
Gender categorical Units: Subjects			
Female	43	44	43
Male	2	3	3

Reporting group values	Placebo	Total	
Number of subjects	45	183	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 42.3 ± 13.04	 -	
Gender categorical Units: Subjects			
Female	38	168	
Male	7	15	

End points

End points reporting groups

Reporting group title	PF-04236921 10 milligram (10 mg)
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	PF-04236921 50 mg
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	PF-04236921 200 mg
Reporting group description:	
Subjects received PF-04236921 subcutaneously in the anterolateral right and left thighs.	
Reporting group title	Placebo
Reporting group description:	
Placebo matching to PF-04236921 administered subcutaneously in the anterolateral right and left thighs.	

Primary: Percentage of Subjects Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 24

End point title	Percentage of Subjects Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 24[1]

End point description:

SRI components: Systemic Lupus Erythematosus Disease Activity Index 2000(SLEDAI 2K),British Isles Lupus Activity Group(BILAG) 2004,Physician’s Global Assessment(PhGA).Subjects classified as responder if they did not meet definition of treatment failure and met all the following criteria: greater than or equal to (>=)4 point reduction in SLEDAI 2K score; no new BILAG A organ domain score/2 new BILAG B organ domain scores; less than (<) 0.3 point increase in PhGA score. Treatment failure: any new/increased use of corticosteroids,immunosuppressants/antimalarial drug,death,hospitalization/treatment discontinuation due to SLE, any flare of lupus interfering with study participation. SLEDAI-2K:assesses improvement in disease activity(0 to 105;higher score=higher severity). BILAG:assesses disease extent, severity (A [severe] to E [no disease]). PhGA: assesses worsening in subject’s general health status(0[none] to 3[severe]). Full Analysis Set (FAS) excluding 200-mg dose group.

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35[2]	36[3]	42[4]	
Units: Percentage of Subjects				
number (not applicable)	59.9	39.2	40.1	

Notes:

[2] - Here, 'N' signifies subjects who completed through the Week 24 visit for each group respectively.

[3] - Here, 'N' signifies subjects who completed through the Week 24 visit for each group respectively.

[4] - Here, 'N' signifies subjects who completed through the Week 24 visit for each group respectively.

Statistical analyses

Statistical analysis title	Analysis for SRI: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the Odds ratio (ORs) as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.076 [5]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.89
upper limit	5.62

Notes:

[5] - P-value was displayed without adjusting for multiplicity.

Statistical analysis title	Analysis for SRI: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.528 [6]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.38
upper limit	2.41

Notes:

[6] - P-value was displayed without adjusting for multiplicity.

Secondary: Percentage of Subjects Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 4, 8, 12, 16, and 20

End point title	Percentage of Subjects Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 4, 8, 12, 16, and 20[7]

End point description:

SRI components: SLEDAI 2K, BILAG 2004, PhGA. Subjects classified as responder if they did not meet definition of treatment failure and met all the following criteria: >=4 point reduction in SLEDAI 2K score; no new BILAG A organ domain score/2 new BILAG B organ domain scores; <0.3 point increase in

PhGA score. Treatment failure: any new/increased use of corticosteroids,immunosuppressants/antimalarial drug,death,hospitalization/treatment discontinuation due to SLE, any flare of lupus interfering with study participation. SLEDAI-2K:assesses improvement in disease activity(0 to 105;higher score=higher severity). BILAG:assesses disease extent, severity (A [severe] to E [no disease]). PhGA: assesses worsening in subject's general health status(0[none] to 3[severe]). Full Analysis Set (FAS) excluding 200-mg dose group; 'n' = subjects evaluable at specified

End point type	Secondary

End point timeframe:

Week 4, 8, 12, 16, 20

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Percentage of Subjects				
number (not applicable)				
Week 4 (n=43, 44, 45)	12.2	7.1	4.8	
Week 8 (n=43, 43, 43)	26.8	21.5	26.3	
Week 12 (n=39, 41, 42)	33.7	20	36.3	
Week 16 (n=36, 39, 41)	48.9	28.9	37.1	
Week 20 (n=36, 39, 43)	54.7	36.8	38.3	

Statistical analyses

Statistical analysis title	Analysis at Week 4: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.62
upper limit	12.4

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized

linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.31
upper limit	7.71

Statistical analysis title	Analysis at Week 8: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4
upper limit	2.67

Statistical analysis title	Analysis at Week 8: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.29
upper limit	2.05

Statistical analysis title	Analysis at Week 12: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.35
upper limit	2.24

Statistical analysis title	Analysis at Week 12: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.44
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.16
upper limit	1.16

Statistical analysis title	Analysis at Week 16: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.64
upper limit	4.09

Statistical analysis title	Analysis at Week 16: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.27
upper limit	1.77

Statistical analysis title	Analysis at Week 20: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.78
upper limit	4.84

Statistical analysis title	Analysis at Week 20: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.38
upper limit	2.32

Secondary: Percentage of Subjects Achieving Modified Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 4, 8, 12, 16, 20, and 24

End point title	Percentage of Subjects Achieving Modified Systemic Lupus Erythematosus (SLE) Responder Index (SRI) at Week 4, 8, 12, 16, 20, and 24[8]

End point description:

SRI components include: modified SLEDAI 2K (SLEDAI 2K without standard parameters "Low complement" and "Leukopenia"), BILAG 2004, PhGA. Subjects classified as responder if they did not meet definition of treatment failure and met all the following criteria: >=4 point reduction in SLEDAI 2K score; no new BILAG A organ domain score or 2 new BILAG B organ domain scores; <0.3 point increase in PhGA score. Treatment failure: any new/increased use of corticosteroids, immunosuppressants/antimalarial drug, death, hospitalization/treatment discontinuation due to SLE, any flare of lupus interfering with study participation. Modified SLEDAI-2K: assesses improvement in disease activity (0 to 102; higher score = higher severity). BILAG: assesses disease extent, severity (A [severe] to E [no disease]). PhGA: assesses worsening in subject's general health status (0[none] to 3[severe]). FAS excluding the subjects in the 200-mg dose group; 'n' = subjects evaluable at specified time point.

End point type	Secondary

End point timeframe:

Week 4, 8, 12, 16, 20, 24

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Percentage of Subjects				
number (not applicable)				
Week 4 (n=43, 44, 45)	9.5	7	9.2	
Week 8 (n=43, 43, 43)	23.8	25.7	30.2	
Week 12 (n=39, 41, 42)	35.6	24.9	42.6	
Week 16 (n=36, 39, 41)	50.2	34	41	

Week 20 (n=36, 39, 43)	56.5	46.9	42.2	
Week 24 (n=35, 36, 42)	61.2	41.4	41.6	

Statistical analyses

Statistical analysis title	Analysis at Week 4: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.28
upper limit	3.88

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.19
upper limit	3.01

Statistical analysis title	Analysis at Week 8: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.28
upper limit	1.85

Statistical analysis title	Analysis at Week 8: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.32
upper limit	2.02

Statistical analysis title	Analysis at Week 12: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.3
upper limit	1.83

Statistical analysis title	Analysis at Week 12: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.18
upper limit	1.13

Statistical analysis title	Analysis at Week 16: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.58
upper limit	3.6

Statistical analysis title	Analysis at Week 16: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 50 mg

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.3
upper limit	1.84

Statistical analysis title	Analysis at Week 20: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 10 milligram (10 mg)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.72
upper limit	4.37

Statistical analysis title	Analysis at Week 20: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5
upper limit	2.92

Statistical analysis title	Analysis at Week 24: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 10 milligram (10 mg)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.89
upper limit	5.55

Statistical analysis title	Analysis at Week 24: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4
upper limit	2.46

Secondary: Percentage of Subjects Achieving British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response at Week 4, 8, 12, 16, 20, and 24

End point title	Percentage of Subjects Achieving British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response at Week 4, 8, 12, 16, 20, and 24[9]

End point description:

BICLA include: BILAG-2004, SLEDAI-2K, PhGA of disease activity. Subjects classified as responder if they did not meet definition of treatment failure and met all the following criteria: BILAG-2004 improvement(all A scores at baseline improved to B/C/D, all B scores improved to C or D); no worsening in disease activity(no new BILAG-2004 A scores or =<1 new B score); no worsening of total SLEDAI-2K score; no <10 percent [%] worsening in analogue PhGA. Treatment failure: any new/increased use of corticosteroids, immunosuppressants/antimalarial, death, hospitalization/treatment discontinuation due to SLE, any flare of lupus interfering with study participation. BILAG:assesses disease extent, severity (A[severe] to E[no disease]). SLEDAI-2K:assesses improvement in disease activity (0 to 105; higher score=higher severity). PhGA: assesses worsening in subject’s general health status(0[none] to 3

[severe]). FAS excluding 200-mg dose group; 'n' = subjects evaluable at specified time point.

End point type	Secondary

End point timeframe:

Week 4, 8, 12, 16, 20, 24

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Percentage of Subjects				
number (not applicable)				
Week 4 (n=43, 44, 45)	26.2	21.7	21	
Week 8 (n=43, 43, 43)	26.2	29	30.6	
Week 12 (n=39, 41, 42)	33.6	39.6	33.3	
Week 16 (n=36, 39, 41)	45.5	39.2	26.2	
Week 20 (n=35, 39, 43)	43.7	31.6	21.7	
Week 24 (n=35, 36, 42)	49.7	40.5	25.1	

Statistical analyses

Statistical analysis title	Analysis at Week 4: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.53
upper limit	3.35

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.41
upper limit	2.65

Statistical analysis title	Analysis at Week 8: PF-04236921 10 mg v. Placebo
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.33
upper limit	1.96

Statistical analysis title	Analysis at Week 8: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.39
upper limit	2.23

Statistical analysis title	Analysis at Week 12: PF-04236921 10 mg v. Placebo
Comparison groups	PF-04236921 50 mg v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.42
upper limit	2.45

Statistical analysis title	Analysis at Week 12: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.55
upper limit	3.1

Statistical analysis title	Analysis at Week 16: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.95
upper limit	5.88

Statistical analysis title	Analysis at Week 16: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.74
upper limit	4.46

Statistical analysis title	Analysis at Week 20: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	Placebo v PF-04236921 10 milligram (10 mg)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.1
upper limit	7.12

Statistical analysis title	Analysis at Week 20: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.67

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.66
upper limit	4.21

Statistical analysis title	Analysis at Week 24: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.18
upper limit	7.41

Statistical analysis title	Analysis at Week 24: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.82
upper limit	5.06

Secondary: Percentage of Subjects Achieving Pre-defined Criteria for Systemic Lupus Erythematosus (SLE) Responder Index (SRI) Components at Week 24

End point title	Percentage of Subjects Achieving Pre-defined Criteria for Systemic Lupus Erythematosus (SLE) Responder Index (SRI) Components at Week 24[10]

End point description:

SRI components: SLEDAI 2K, BILAG 2004, PhGA. Subjects classified as responder if they did not meet definition of treatment failure, met all the following criteria: >=4 point reduction in SLEDAI 2K score; no new BILAG A organ domain score/2 new BILAG B organ domain scores;<0.3 point increase in PhGA score. Treatment failure: any new/increased use of corticosteroids,immunosuppressants/antimalarial drug,death, hospitalization/treatment discontinuation due to SLE,any flare of lupus interfering with study participation. SLEDAI-2K:assesses improvement in disease activity(0 to 105;higher score=higher severity).BILAG:assesses disease extent, severity (A[severe] to E[no disease]). PhGA: assesses worsening in subject's general health (0[none] to 3[severe]). FAS excluding 200-mg dose group; 'n' = subjects evaluable for specified categories. Model percent estimates reported only for 'Reduction in SLEDAI Score', 'No Worsening in PhGA' categories; for remaining categories, raw percentages reported.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34[11]	36[12]	41[13]	
Units: Percentage of Subjects				
number (not applicable)				
4 or More Points Reduction in SLEDAI Score	60.7	44.9	49.3	
No New 1A/2B BILAG	100	100	90.2	
No Worsening in PhGA	97.4	97.5	93.1	
Treatment Failure	0	2.8	4.9	

Notes:

[11] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[12] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[13] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

Statistical analyses

Statistical analysis title	SLEDAI component: PF-04236921 10 mg v. Placebo

Statistical analysis description:

>=4 points reduction in SLEDAI score: Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 [14]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.59

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.63
upper limit	4.02

Notes:

[14] - P-value was displayed without adjusting for multiplicity.

Statistical analysis title	SLEDAI Component: PF-04236921 50 mg v. Placebo

Statistical analysis description:

>=4 points reduction in SLEDAI score: Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.625 [15]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.34
upper limit	2.08

Notes:

[15] - P-value was displayed without adjusting for multiplicity.

Statistical analysis title	PhGA Component: PF-04236921 10 mg v. Placebo

Statistical analysis description:

No worsening in PhGA: Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198 [16]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.38
upper limit	20.65

Notes:

[16] - P-value was displayed without adjusting for multiplicity.

Statistical analysis title	PhGA Component: PF-04236921 10 mg v. Placebo

Statistical analysis description:

No worsening in PhGA: Point estimates of the ORs as well as their confidence intervals were calculated from the generalized linear mix model that included fixed factors of the stratification factors, treatment, visit and treatment by visit.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.192 [17]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	2.88
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.39
upper limit	21.3

Notes:

[17] - P-value was displayed without adjusting for multiplicity.

Secondary: Number of Subjects With Clinically Significant Laboratory Tests Results

End point title	Number of Subjects With Clinically Significant Laboratory Tests Results

End point description:

Pre-defined criteria were established for each laboratory test to define values that would be identified as of potential clinical importance. Laboratory values included Alanine Aminotransferase(ALT) [>5.0-10.0*Upper limit of normal range(ULN)], Albumin[<26-20 gram per liter(g/L)/<20 g/L], Amylase[>2.0-5.0*ULN], Aspartate Aminotransferase (AST)[>5.0-10.0*ULN], Creatine Kinase(CK)[>5.0-10.0*ULN/ >10.0*ULN], Glucose(Hyperglycemia)[>13.9-27.8millimoles/liter(mmol/L)],Hemoglobin(HGB)[<80-65g/L/<65g/L],Lipase[>2.0-5.0*ULN], Lymphocytes(Lymph.)(Absolute[Abs])[<0.5-0.2*10^3/microliter(UL)/<0.2*10^3/UL],Platelets[<50-25*10^3/UL/<25*10^3/UL],potassium (low)[<3.0-2.5 mmol/L], Sodium(low)[<130-120 mmol/L], Total Neutrophils(TN) (Abs)[<1.0-0.5*10^3/UL/ <0.5*10^3/UL], Triglycerides[>5.7-11.4 mmol/L], White Blood Cell Count(WBC)[<2.0-1.0*10^3/UL/<1.0*10^3/UL]. Safety population: all subjects who had at least 1 dose of investigational product; 'n'= subjects evaluable for specified parameter.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects				
ALT (n=45, 47, 45, 45)	2	0	0	0
Albumin: <26-20 g/L (n=45, 47, 45, 45)	1	1	1	1
Albumin: <20 g/L (n=45, 47, 45, 45)	0	1	0	0
Amylase (n=45, 47, 45, 45)	1	1	1	1
AST (n=45, 47, 45, 45)	0	1	0	1
CK: >5.0 -10.0*ULN (n=45,47,45,45)	0	1	1	0
CK >10.0*ULN (n=45,47,45,45)	0	1	1	0

Glucose (Hyperglycemia) (n=45,47,45,45)	1	1	0	2
HGB: <80 - 65 g/L (n=45,47,45,45)	1	0	0	1
HGB: <65 g/L (n=45,47,45,45)	1	0	0	0
Lipase (n=45,47,45,45)	0	1	1	0
Lymph.(Abs)<0.5-0.2* 10^3/UL(n=45,47,45,45)	6	9	4	8
Lymphocytes (Abs) <0.2*10^3/UL (n=45,47,45,45)	1	0	0	0
Platelets <50 - 25*10^3/UL (n=45,47,45,45)	0	0	0	2
Platelets <25*10^3/UL (n=45,47,45,45)	0	0	0	1
Potassium (low) (n=45,47,45,45)	2	1	1	1
Sodium (low) (n=45,47,45,45)	0	0	1	0
TN (Abs)<1.0-0.5*10^3/UL (n=45,47,45,45)	4	5	3	2
TN (Abs) <0.5*10^3/UL (n=45,47,45,45)	1	1	1	0
Triglycerides (n=44,47,45,45)	0	1	0	2
WBC <2.0 - 1.0*10^3/UL (n=45,47,45,45)	4	2	2	2
WBC <1.0*10^3/UL (n=45,47,45,45)	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Discontinued due to Adverse Events

End point title	Number of Subjects who Discontinued due to Adverse Events

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An 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. Number of subjects who discontinued due to AEs were reported. Safety population defined as all subjects who had at least one dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects	3	2	3	3

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An 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 52 that were absent before treatment or that worsened relative to pretreatment state. Number of subjects with treatment-emergent AEs or SAEs (excluding infectious AEs or SAEs) were reported. AEs include both SAEs and non-SAEs.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects				
AEs	34	36	38	40
SAEs	4	2	7	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Infectious Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-Emergent Infectious Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An 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 52 that were absent before treatment or that worsened relative to pretreatment state. Number of subjects with treatment-emergent infectious AEs or SAEs were reported. AEs include both SAEs and non-SAEs. Safety population defined as all subjects who had at least one dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects				
Infectious AEs	25	28	25	26
Infectious SAEs	2	3	4	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Important (PCI) Electrocardiogram (ECG) Findings

End point title	Number of Subjects With Potentially Clinically Important (PCI) Electrocardiogram (ECG) Findings

End point description:

Criteria for PCI findings in ECG were defined as: heart rate <=40 beats per minute (bpm) or >=120 bpm; PR interval >=220 millisecond (msec); QT interval >=480 msec; QRS interval >=120 msec; QT interval corrected using the Fridericia formula (QTcF) >=500msec; no sinus rhythm. Safety population defined as all subjects who had at least one dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42[18]	46[19]	44[20]	44[21]
Units: Subjects				
Heart Rate <=40 beats/min or >=120 beats/min	0	0	0	0
PR Interval >=200 msec	2	1	1	2
QT Interval >=480 msec	2	0	0	0
QRS Interval >=120 msec	3	1	2	2
QTcF >=500 msec	2	0	0	0
Rhythm (Not Sinus Rhythm)	0	0	0	1

Notes:

[18] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[19] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[20] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[21] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Important Vital Signs Findings

End point title	Number of Subjects With Potentially Clinically Important Vital Signs Findings

End point description:

Criteria for PCI findings in vital signs were defined as: sitting systolic blood pressure (Increase from baseline >=20 millimeter of mercury (mm Hg) and >=160 mm Hg or a decrease from baseline >=20 mm Hg and <=90 mm Hg) and sitting diastolic blood pressure (increase from baseline >=15 mm Hg and >=90 mm Hg or decrease from baseline >=15 mm Hg and <=60 mm Hg), pulse rate (increase from baseline >=15 beats/min and >=120 beats/min or decrease from baseline >=15 beats/min and <=50 beats /min), body temperature (increase of >=2 degree Fahrenheit (F) and temperature >=101 degree F) and weight (change of >=7% in body weight). Safety population defined as all subjects who had at least one dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects				
Sitting Systolic Blood Pressure	8	3	3	5
Sitting Diastolic Blood Pressure	14	14	12	14
Sitting Pulse Rate	1	1	0	1
Temperature	0	0	0	0
Weight	12	23	14	14

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (Nabs)

End point title	Number of Subjects With Anti-drug Antibodies (ADAs) and Neutralizing Antibodies (Nabs)

End point description:

Human serum samples were analyzed for the presence or absence of anti-PF-04236921 antibodies. A positive ADA sample was further tested for neutralizing antibodies using a validated assay. Safety population defined as all subjects who had at least one dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	46	45
Units: Subjects				
Anti-drug Antibodies	1	0	1	0
Neutralizing Antibodies	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of PF-04236921

End point title	Serum concentration of PF-04236921[22]

End point description:

Serum PF-04236921 concentrations over time were summarized. Pharmacokinetic analysis set was the subset of subjects from safety analysis set (all subjects who received at least 1 dose of investigational product) who provided at least 1 pharmacokinetic concentration. Here, 'n' signifies number of observations (non-missing concentrations) at the specified time points for each group respectively.

End point type	Secondary

End point timeframe:

Day 1, Week 2, 4, 6, 8, 12, 16, 20, 24

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Serum concentration of PF-04236921 was not planned to be reported for placebo group.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	46	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=42, 45, 43)	26.3 (± 110.8)	31 (± 146.9)	15.2 (± 99.8)	
Week 2 (n=37, 41, 40)	1297 (± 759.4)	5640 (± 2274)	22780 (± 9896)	
Week 4 (n=39, 42, 38)	991.8 (± 527.6)	4337 (± 1495)	17550 (± 5757.1)	
Week 6 (n=39, 40, 37)	608.4 (± 330.1)	3396 (± 1410)	13460 (± 5416.6)	
Week 8 (n=39, 38, 30)	463.4 (± 254.9)	2709 (± 1317.5)	11110 (± 5023.7)	
Week 12 (n=32, 33, 28)	1210 (± 607)	6482 (± 2487.4)	25240 (± 8114)	
Week 16 (n=31, 36, 23)	703.2 (± 407.4)	3886 (± 1322.1)	16990 (± 6203.4)	

Week 20 (n=30, 34, 17)	1452 (± 726.8)	6978 (± 2954)	31050 (± 11368)	
Week 24 (n=31, 34, 18)	871.9 (± 450.4)	4417 (± 2402.4)	20150 (± 12091)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Corticosteroid Dose Reduced by Both Greater Than or Equal to (>=) 25 Percent (%) From Baseline and Less Than or Equal to (<=) 7.5 Milligrams per day (mg/day)

End point title	Percentage of Subjects With Corticosteroid Dose Reduced by Both Greater Than or Equal to (>=) 25 Percent (%) From Baseline and Less Than or Equal to (<=) 7.5 Milligrams per day (mg/day)[23]

End point description:

Subjects were given supplemental corticosteroids at baseline to control disease activity. The steroid taper was based on subject's symptoms. Subjects recorded their steroid usage on a diary card. FAS excluding subjects in 200-mg dose group; Least Observation Carried Forward(LOCF) method was used to impute missing data.

End point type	Secondary

End point timeframe:

Week 12, 16, 20, 24

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	PF-04236921 200 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15[24]	24[25]	23[26]	
Units: Percentage of Subjects				
number (not applicable)				
Week 12	13.3	20.8	8.7	
Week 16	20	25	8.7	
Week 20	26.7	25	8.7	
Week 24	26.7	20.8	8.7	

Notes:

[24] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[25] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[26] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Normalized Serological Activity

End point title	Percentage of Subjects With Normalized Serological Activity[27]

End point description:

Serologic activity was to be assessed in the subgroup of subjects who had positive serologic activity at baseline.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[28]	0[29]	0[30]	
Units: Percentage of Subjects				
number (not applicable)				

Notes:

[28] - Data was not analyzed as number of subjects with abnormal values at baseline was minimal (<=25%).
[29] - Data was not analyzed as number of subjects with abnormal values at baseline was minimal (<=25%).
[30] - Data was not analyzed as number of subjects with abnormal values at baseline was minimal (<=25%).

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Visual Analog Scale (VAS) Scores at Baseline

End point title	Patient Global Visual Analog Scale (VAS) Scores at Baseline[31]

End point description:

Subjects assessed their disease activity using a 100 mm VAS. Subjects answered the following question "Considering all the ways your disease affects you, how are you feeling today?" Response was recorded by placing a mark on the scale between 0 (very well) and 100 (extremely bad). FAS excluding the subjects in the 200-mg dose group.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: mm				
arithmetic mean (standard error)	50.44 (± 2.865)	47.7 (± 2.88)	49.47 (± 3.349)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Visual Analog Scale (VAS) at Week 2, 4, 6, 8, 12, 16, 20 and 24

End point title	Change From Baseline in Patient Global Visual Analog Scale (VAS) at Week 2, 4, 6, 8, 12, 16, 20 and 24[32]

End point description:

Subjects assessed their disease activity using a 100 mm VAS. Subjects answered the following question "Considering all the ways your disease affects you, how are you feeling today?" Response was recorded by placing a mark on the scale between 0 (very well) and 100 (extremely bad). FAS excluding the subjects in the 200-mg dose group; 'n' =subjects evaluable at specified time point. LOCF method was used to impute missing values.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 20, 24

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: mm				
least squares mean (confidence interval 95%)				
Week 2 (n=44, 47, 43)	-9.17 (-15.09 to -3.26)	-1.54 (-7.22 to 4.15)	-3.58 (-9.49 to 2.34)	
Week 4 (n=45, 47, 45)	-3.24 (-9.09 to 2.62)	-4.01 (-9.69 to 1.68)	-1.24 (-7.02 to 4.55)	
Week 6 (n=45, 47, 45)	-5.48 (-11.33 to 0.37)	-3.62 (-9.31 to 2.06)	-7.24 (-13.02 to -1.45)	
Week 8 (n=45, 47, 45)	-4.17 (-10.02 to 1.68)	-6.03 (-11.71 to -0.34)	-7.11 (-12.89 to -1.32)	
Week 12 (n=45, 47, 45)	-9.21 (-15.07 to -3.36)	-4.2 (-9.88 to 1.49)	-6.88 (-12.67 to -1.1)	
Week 16 (n=45, 47, 45)	-8.75 (-14.6 to -2.89)	-10.2 (-15.88 to -4.51)	-5.99 (-11.78 to -0.21)	
Week 20 (n=45, 47, 45)	-11.52 (-17.38 to -5.67)	-9.03 (-14.71 to -3.34)	-6.77 (-12.56 to -0.99)	
Week 24 (n=45, 47, 45)	-9.17 (-15.02 to -3.32)	-7.45 (-13.14 to -1.77)	-10.64 (-16.42 to -4.85)	

Statistical analyses

Statistical analysis title	Analysis at Week 2: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-5.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.3
upper limit	1.49

Statistical analysis title	Analysis at Week 4: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 10 milligram (10 mg)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-1.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.21
upper limit	5.42

Statistical analysis title	Analysis at Week 6: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	1.3

Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.71
upper limit	8.32

Statistical analysis title	Analysis at Week 8: PF-04236921 10 mg v. Placebo
Statistical analysis description:	
Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	4.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.22
upper limit	11.57

Statistical analysis title	Analysis at Week 12: PF-04236921 10 mg v. Placebo
Statistical analysis description:	
Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-3.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.04
upper limit	3.07

Statistical analysis title	Analysis at Week 16: PF-04236921 10 mg v. Placebo
Statistical analysis description:	
Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-2.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.87
upper limit	4.1

Statistical analysis title	Analysis at Week 20: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-6.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.37
upper limit	0.94

Statistical analysis title	Analysis at Week 24: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	1.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.17
upper limit	9.13

Statistical analysis title	Analysis at Week 2: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	2.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.7
upper limit	8.84

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-2.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.62
upper limit	4

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	3.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.95
upper limit	10.9

Statistical analysis title	Analysis at Week 8: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	2.56
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.29
upper limit	9.4

Statistical analysis title	Analysis at Week 12: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	3.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.67
upper limit	9.94

Statistical analysis title	Analysis at Week 16: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-4.94

Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.91
upper limit	2.03

Statistical analysis title	Analysis at Week 20: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	-2.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.61
upper limit	4.32

Statistical analysis title	Analysis at Week 24: PF-04236921 50 mg v.Placebo

Statistical analysis description:

Analysis was done using linear mixed effect model that included fixed factors of the stratification factors, treatment, visit, treatment by visit and baseline VAS.

Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS Mean difference
Point estimate	2.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.48
upper limit	9.8

Secondary: Change From Baseline in European Quality of Life 5 Dimensions Questionnaire (EQ-5D) at Week 4, 8, 12, 16, 20 and 24

End point title	Change From Baseline in European Quality of Life 5 Dimensions Questionnaire (EQ-5D) at Week 4, 8, 12, 16, 20 and 24[33]

End point description:

EQ-5D is a standardized, subject-administered measure of health outcome. It provides a descriptive profile for 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), using

3 levels (no, moderate, or extreme problems) and a single index value characterizing current health status using a 100-point VAS (0= worst imaginable health state, 100= best imaginable health state).

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[34]	0[35]	0[36]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[34] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

[35] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

[36] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

Statistical analyses

No statistical analyses for this end point

Secondary: Thirty six-Item Short-Form Health Survey (SF-36) Physical Component Score (PCS) and Mental Component Score (MCS) at Baseline

End point title	Thirty six-Item Short-Form Health Survey (SF-36) Physical Component Score (PCS) and Mental Component Score (MCS) at Baseline[37]

End point description:

SF-36 is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as PCS and MCS. The score for each aspect and PCS/MCS is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). FAS excluding the subjects in the 200-mg dose group.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43[38]	46[39]	45	
Units: Units on a scale				
arithmetic mean (standard error)				
MCS	39.5 (± 1.81)	42.36 (± 1.426)	39.94 (± 1.45)	

PCS	33.47 (± 1.169)	34.36 (± 1.25)	34.64 (± 1.523)	

Notes:

[38] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

[39] - Here, 'N' signifies subjects evaluable for this end point for each group respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 36-Item Short-Form Health Survey (SF-36) PCS and MCS at Week 4, 8, 12, 16, 20 and 24

End point title	Change From Baseline in 36-Item Short-Form Health Survey (SF-36) PCS and MCS at Week 4, 8, 12, 16, 20 and 24[40]

End point description:

SF-36 is a standardized survey evaluating 8 aspects of functional health and well-being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. These 8 aspects can also be summarized as PCS and MCS. The score for each aspect and PCS/MCS is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). LOCF method was used to impute missing values. Here,
'n' =subjects evaluable at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Units on a scale				
least squares mean (confidence interval 95%)				
MCS: Week 4 (n=43, 45, 45)	1.97 (-0.69 to 4.64)	1.45 (-1.14 to 4.04)	1.45 (-1.12 to 4.02)	
MCS: Week 8 (n=43, 46, 45)	1.57 (-1.1 to 4.23)	1.97 (-0.59 to 4.52)	2.05 (-0.52 to 4.62)	
MCS: Week 12 (n=43, 46, 45)	3.8 (1.13 to 6.46)	2.5 (-0.06 to 5.05)	2.52 (-0.05 to 5.09)	
MCS: Week 16 (n=43, 46, 45)	4.73 (2.07 to 7.4)	2.79 (0.24 to 5.35)	2.95 (0.38 to 5.52)	
MCS: Week 20 (n=43, 46, 45)	4.49 (1.82 to 7.15)	1.71 (-0.85 to 4.26)	3.28 (0.71 to 5.85)	
MCS: Week 24 (n=43, 46, 45)	2.94 (0.28 to 5.6)	2.14 (-0.41 to 4.7)	2.85 (0.28 to 5.42)	
PCS: Week 4 (n=43, 45, 45)	3.95 (1.75 to 6.15)	3.24 (1.1 to 5.38)	1.28 (-0.85 to 3.4)	
PCS: Week 8 (n=43, 46, 45)	5.48 (3.27 to 7.68)	4.79 (2.68 to 6.9)	2.11 (-0.01 to 4.23)	
PCS: Week 12 (n=43, 46, 45)	6.06 (3.86 to 8.26)	4.66 (2.55 to 6.77)	2.82 (0.7 to 4.95)	

PCS: Week 16 (n=43, 46, 45)	6.25 (4.05 to 8.45)	4.5 (2.39 to 6.61)	2.48 (0.36 to 4.6)	
PCS: Week 20 (n=43, 46, 45)	6.39 (4.19 to 8.59)	5.63 (3.52 to 7.74)	3.29 (1.17 to 5.42)	
PCS: Week 24 (n=43, 46, 45)	5.98 (3.77 to 8.18)	5.53 (3.42 to 7.64)	2.94 (0.82 to 5.06)	

Statistical analyses

Statistical analysis title	MCS Analysis Week 4: PF-04236921 10 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.53
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.53
upper limit	3.59

Statistical analysis title	MCS Analysis Week 8: PF-04236921 10 mg vs Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-0.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.54
upper limit	2.58

Statistical analysis title	MCS Analysis Week 16: PF-04236921 10 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.28
upper limit	4.84

Statistical analysis title	MCS Analysis Week 12:PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.28
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.78
upper limit	4.34

Statistical analysis title	MCS Analysis Week 20: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.86
upper limit	4.26

Statistical analysis title	MCS Analysis Week 24: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.98
upper limit	3.15

Statistical analysis title	MCS Analysis Week 4: PF-04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.03
upper limit	3.03

Statistical analysis title	MCS Analysis Week 8: PF-04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-0.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.09
upper limit	2.92

Statistical analysis title	MCS Analysis Week 12: PF-04236921 50 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.03
upper limit	2.99

Statistical analysis title	MCS Analysis Week 16: PF-04236921 50 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-0.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.17
upper limit	2.85

Statistical analysis title	MCS Analysis Week 20: PF-04236921 50 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-1.58
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.58
upper limit	1.43

Statistical analysis title	MCS Analysis Week 24: PF-04236921 50 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	-0.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.72
upper limit	2.3

Statistical analysis title	PCS Analysis Week 4: PF-04236921 10 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.14
upper limit	5.2

Statistical analysis title	PCS Analysis Week 8: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.84
upper limit	5.89

Statistical analysis title	PCS Analysis Week 12: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	5.76

Statistical analysis title	PCS Analysis Week 16: PF-04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.24
upper limit	6.3

Statistical analysis title	PCS Analysis Week 20: PF-04236921 10 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.57
upper limit	5.63

Statistical analysis title	PCS Analysis Week 24: PF-04236921 10 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5
upper limit	5.56

Statistical analysis title	PCS Analysis Week 4: PF-04236921 50 mg v Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.96

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.53
upper limit	4.46

Statistical analysis title	PCS Analysis Week 8: PF-04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.68
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.2
upper limit	5.17

Statistical analysis title	PCS Analysis Week 12: PF-04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.65
upper limit	4.32

Statistical analysis title	PCS Analysis Week 16: PF-04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.47
upper limit	4.5

Statistical analysis title	PCS Analysis Week 20: PF-04236921 50 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.34
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.15
upper limit	4.82

Statistical analysis title	PCS Analysis Week 24: PF-04236921 50 mg v Placebo
Statistical analysis description:	
Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.59
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.11
upper limit	5.08

Secondary: Change From Baseline in Vitality Scores at Week 4, 8, 12, 16, 20 and 24

End point title	Change From Baseline in Vitality Scores at Week 4, 8, 12, 16, 20 and 24[41]

End point description:

SF-36 is a standardized survey evaluating 8 aspects of functional health and well being: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. Vitality sub-score is a component of SF-36 Health Survey Questionnaire and assesses energy and fatigue. The vitality score ranged from 0-100 (100=highest level of functioning). FAS excluding the subjects in the 200-mg dose group. LOCF method was used to impute missing values. As the SF-36 MCS component results were not significant at any timepoint, the decision was made to evaluate the vitality domain, at only Week 24 timepoint. Here, results for only Week 24 time point are reported.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	46	45	
Units: Units on a scale				
least squares mean (standard error)	10.3 (± 3.088)	7.45 (± 2.983)	6.42 (± 3.022)	

Statistical analyses

Statistical analysis title	Vitality Analysis: PF04236921 10 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the treatment difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.374
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.71
upper limit	12.46

Statistical analysis title	Vitality Analysis: PF04236921 50 mg v Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the treatment difference from that

model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.81
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	9.46

Secondary: Change From Baseline in Short Form-6 Dimension (SF-6D) at Week 4, 8, 12, 16, 20 and 24

End point title	Change From Baseline in Short Form-6 Dimension (SF-6D) at Week 4, 8, 12, 16, 20 and 24[42]

End point description:

The SF-6D focuses on seven of the eight health domains covered by the SF-36 version2(v2) Health Survey: physical functioning, role participation (combined role-physical and role-emotional), social functioning, bodily pain, mental health, and vitality. Only the general health domain is not included. The SF-6D index is scored from 0.0 (worst health state) to 1.0 (best health state).

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[43]	0[44]	0[45]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[43] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

[44] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

[45] - Data was not analyzed as SF-36 scale was sufficient for evaluating subject reported quality of life.

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) Score at Baseline

End point title	Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) Score at Baseline[46]

End point description:

FACIT-F is a 13-item questionnaire. Subjects scored each item on a 5-point scale: 0 (not at all) to 4 (very much). Larger the subject's response to the questions (with the exception of 2 negatively stated), greater was the subject's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the subject's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). FAS excluding the subjects in the 200-mg dose group.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Units on a scale				
arithmetic mean (standard deviation)	25.91 (± 1.7)	29.38 (± 1.506)	25.96 (± 1.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) Score at Week 4, 8, 12, 16, 20 and 24

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) Score at Week 4, 8, 12, 16, 20 and 24[47]

End point description:

FACIT-F is a 13-item questionnaire. Subjects scored each item on a 5-point scale: 0 (not at all) to 4 (very much). Larger the subject's response to the questions (with the exception of 2 negatively stated), greater was the subject's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the subject's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). Here, 'n' signifies subjects evaluable for this end point at the specified time points. LOCF method was used to impute missing values.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per planned analysis, for this end point, FAS population excluding the subjects in 200 mg group was used. Hence, the arm "PF-04236921 200 mg" was excluded from the analysis.

End point values	PF-04236921 10 milligram (10 mg)	PF-04236921 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	45	
Units: Units on a scale				
least squares mean (confidence interval 95%)				
Week 4 (n=43, 45, 45)	3.16 (0.25 to 6.07)	2.77 (-0.05 to 5.6)	1.08 (-1.72 to 3.89)	
Week 8 (n=43, 46, 45)	4.39 (1.49 to 7.3)	3.41 (0.62 to 6.2)	2.44 (-0.37 to 5.24)	
Week 12 (n=43, 46, 45)	5.07 (2.16 to 7.97)	3.59 (0.8 to 6.38)	2.26 (-0.54 to 5.06)	
Week 16 (n=43, 46, 45)	5.81 (2.9 to 8.72)	5.53 (2.74 to 8.32)	1.93 (-0.88 to 4.73)	
Week 20 (n=43, 46, 45)	5.37 (2.46 to 8.28)	4.32 (1.53 to 7.11)	3.42 (0.61 to 6.22)	
Week 24 (n=43, 46, 45)	4.39 (1.49 to 7.3)	3.3 (0.51 to 6.09)	2.7 (-0.1 to 5.51)	

Statistical analyses

Statistical analysis title	Analysis at Week 4: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the Least Square (LS) mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.26
upper limit	5.42

Statistical analysis title	Analysis at Week 8: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.38
upper limit	5.29

Statistical analysis title	Analysis at Week 12: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	2.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.53
upper limit	6.15

Statistical analysis title	Analysis at Week 16: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.88
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.54
upper limit	7.22

Statistical analysis title	Analysis at Week 20: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.39
upper limit	5.29

Statistical analysis title	Analysis at Week 24: PF-04236921 10 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 10 milligram (10 mg) v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.65
upper limit	5.03

Statistical analysis title	Analysis at Week 4: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.61
upper limit	4.99

Statistical analysis title	Analysis at Week 8: PF-04236921 50 mg v. Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.31
upper limit	4.26

Statistical analysis title	Analysis at Week 12: PF-04236921 50 mg v. Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	1.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.96
upper limit	4.61

Statistical analysis title	Analysis at Week 16: PF-04236921 50 mg v. Placebo
Statistical analysis description: Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.	
Comparison groups	Placebo v PF-04236921 50 mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	3.6

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.32
upper limit	6.89

Statistical analysis title	Analysis at Week 20: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.91
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.38
upper limit	4.19

Statistical analysis title	Analysis at Week 24: PF-04236921 50 mg v. Placebo

Statistical analysis description:

Analysis was done using the ANCOVA model; CI parameter being the LS mean difference from that model.

Comparison groups	PF-04236921 50 mg v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.68
upper limit	3.88

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/SAEs were collected from baseline up to Week 52

Adverse event reporting additional description:

An AE may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study. SAEs consist of all the SAEs including infectious SAEs; non-SAEs consist of all the non-SAEs including infectious non-SAEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	PF-04236921 10 mg

Reporting group description:

Subjects received 10 mg dose of PF-04236921 subcutaneously in the anterolateral right and left thighs at Week 0, Week 8 and Week 16.

Reporting group title	PF-04236921 50 mg

Reporting group description:

Subjects received 50 mg dose of PF-04236921 subcutaneously in the anterolateral right and left thighs at Week 0, Week 8 and Week 16.

Reporting group title	PF-04236921 200 mg

Reporting group description:

Subjects received 200 mg dose of PF-04236921 subcutaneously in the anterolateral right and left thighs at Week 0, Week 8 and Week 16.

Reporting group title	Placebo

Reporting group description:

Placebo matching to PF-04236921 administered subcutaneously in the anterolateral right and left thighs at Week 0, Week 8 and Week 16.

Serious adverse events	PF-04236921 10 mg	PF-04236921 50 mg	PF-04236921 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 45 (8.89%)	3 / 47 (6.38%)	7 / 46 (15.22%)
number of deaths (all causes)	1	0	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haemorrhage			

subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	2 / 46 (4.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 2
Investigations			
Arthroscopy			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial ischaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Headache			

subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis cerebral			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia, obstructive			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Systemic lupus erythematosus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

Infectious mononucleosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Latent tuberculosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis chronic			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 45 (17.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metrorrhagia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			

subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian haemorrhage				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Arthroscopy				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardio				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vasculitis cerebral			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia, obstructive			

subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Disseminated tuberculosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Latent tuberculosis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis chronic				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	PF-04236921 10 mg	PF-04236921 50 mg	PF-04236921 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 45 (44.44%)	24 / 47 (51.06%)	32 / 46 (69.57%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 45 (8.89%)	2 / 47 (4.26%)	4 / 46 (8.70%)
occurrences (all)	4	2	4
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	2 / 46 (4.35%)
occurrences (all)	0	3	2
Pyrexia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 47 (4.26%)	0 / 46 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	1 / 46 (2.17%)
occurrences (all)	1	1	1
Oropharyngeal pain			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	4 / 46 (8.70%)
occurrences (all)	1	1	4
Cough			
subjects affected / exposed	4 / 45 (8.89%)	1 / 47 (2.13%)	1 / 46 (2.17%)
occurrences (all)	4	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	3 / 46 (6.52%)
occurrences (all)	1	1	3
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	3 / 45 (6.67%)	1 / 47 (2.13%)	2 / 46 (4.35%)
occurrences (all)	3	1	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	2 / 46 (4.35%)
occurrences (all)	1	3	2
Headache			
subjects affected / exposed	4 / 45 (8.89%)	8 / 47 (17.02%)	5 / 46 (10.87%)
occurrences (all)	4	8	5
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 45 (4.44%)	3 / 47 (6.38%)	2 / 46 (4.35%)
occurrences (all)	2	3	2
Abdominal pain upper			
subjects affected / exposed	3 / 45 (6.67%)	0 / 47 (0.00%)	1 / 46 (2.17%)
occurrences (all)	3	0	1
Diarrhoea			
subjects affected / exposed	2 / 45 (4.44%)	3 / 47 (6.38%)	5 / 46 (10.87%)
occurrences (all)	2	3	5
Nausea			
subjects affected / exposed	3 / 45 (6.67%)	4 / 47 (8.51%)	6 / 46 (13.04%)
occurrences (all)	3	4	6
Vomiting			
subjects affected / exposed	1 / 45 (2.22%)	2 / 47 (4.26%)	2 / 46 (4.35%)
occurrences (all)	1	2	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	3 / 46 (6.52%)
occurrences (all)	1	1	3
Pruritus			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	0 / 46 (0.00%)
occurrences (all)	1	1	0

Rash			
subjects affected / exposed	0 / 45 (0.00%)	2 / 47 (4.26%)	4 / 46 (8.70%)
occurrences (all)	0	2	4
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	0 / 46 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 45 (2.22%)	4 / 47 (8.51%)	3 / 46 (6.52%)
occurrences (all)	1	4	3
Back pain			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	3 / 46 (6.52%)
occurrences (all)	1	3	3
Flank pain			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	0 / 46 (0.00%)
occurrences (all)	0	3	0
Pain in extremity			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	4 / 46 (8.70%)
occurrences (all)	0	1	4
Systemic lupus erythematosus			
subjects affected / exposed	3 / 45 (6.67%)	5 / 47 (10.64%)	2 / 46 (4.35%)
occurrences (all)	3	5	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 45 (11.11%)	6 / 47 (12.77%)	3 / 46 (6.52%)
occurrences (all)	5	7	4
Gastroenteritis			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	2 / 46 (4.35%)
occurrences (all)	1	3	5
Pharyngitis			
subjects affected / exposed	2 / 45 (4.44%)	3 / 47 (6.38%)	2 / 46 (4.35%)
occurrences (all)	2	3	2
Sinusitis			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	4 / 46 (8.70%)
occurrences (all)	1	3	5

Upper respiratory tract infection			
subjects affected / exposed	5 / 45 (11.11%)	6 / 47 (12.77%)	11 / 46 (23.91%)
occurrences (all)	8	6	13
Urinary tract infection			
subjects affected / exposed	8 / 45 (17.78%)	5 / 47 (10.64%)	3 / 46 (6.52%)
occurrences (all)	8	9	3
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 45 (2.22%)	4 / 47 (8.51%)	1 / 46 (2.17%)
occurrences (all)	1	4	1
Hyperglycaemia			
subjects affected / exposed	3 / 45 (6.67%)	0 / 47 (0.00%)	2 / 46 (4.35%)
occurrences (all)	3	0	2
Hypertriglyceridaemia			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	3 / 46 (6.52%)
occurrences (all)	1	3	3
Hypoglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 45 (57.78%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Cough subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Investigations Hepatic enzyme increased subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Headache subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Abdominal pain upper			

subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Pain in extremity			

subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Systemic lupus erythematosus			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	6		
Sinusitis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	15		
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Hypoglycaemia			

subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2011	1. Changed primary endpoint of subjects achieving SLE responder Index from Week 20 or 24 to Week 24 only. 2. Combined BILAG, SLEDAI-2K and Physician's Global Assessment endpoints into a single endpoint of components and disposition of SRI. Added corticosteroid taper endpoint. Added endpoint for normalized serologic activity Endpoints. Clarified mean change in patient global VAS, EQ-5D, SF-36 PCS, MCS and Vitality Score –all domains over time including SF-6D, FACIT. 3. AE assessment section was modified to include the monitoring of hypersensitivity reactions to the investigational product.
01 March 2013	1. Due to new safety data, tuberculosis (TB) testing was added at week 12, 24, 36 and week 52 throughout the study. 2. New safety language regarding neutrophil monitoring and monitoring of tuberculosis was added. Subjects were re-evaluated at frequent intervals to monitor the absolute neutrophil counts (ANC) and for signs or symptoms of infections. If the ANC counts increased to >=750 cells per cubic millimeter (cells/mm^3) within 15 days of the next dose at either Week 8 or Week 16, the subject was discontinued and entered the follow up period. Subjects were also discontinued if they developed any symptoms or signs of febrile neutropenia during this period. Following follow up measures were added to this protocol to ensure the continued safety of subjects and to further mitigate the risk of TB infection: a) Serial TB testing (Purified Protein Derivative [PPD] or quantiferon test [QFT]) was implemented to monitor for new cases of TB during the course of study. b) Subjects were carefully monitored throughout study for signs, symptoms of TB such as chest pain, difficulty breathing, wheezing, fever, coughing up mucus or blood, excessive sweating(especially at night), lymphadenopathy, new fatigue, or new unplanned weight loss. c) If a subject converted from a negative to positive TB test during trial by serial testing, they were thoroughly evaluated to exclude TB. d) If it was confirmed that a subject had developed latent or active TB in the study based upon above evaluations, the subject received further doses of test article, and was treated standard antimycobacterial therapy. e) If treatment with steroids was required to treat a documented lupus flare, or intercurrent medical condition, a thorough evaluation was performed to exclude TB infection prior to initiating steroid therapy.
30 April 2013	Further dosing in the 200 mg treatment arm was stopped due to safety reasons and excluded from the primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported