



Clinical trial results:

A 24-Week Randomized, Double Blind, Parallel Group, Active Comparator, Multicenter Study to Assess the Efficacy and Safety of PF-06650833, PF-06651600 (Ritlecitinib) and Tofacitinib Alone and in Combination in Participants With Moderately Severely Active Rheumatoid Arthritis (RA) With an Inadequate Response to Methotrexate Summary

EudraCT number	2019-002676-14
Trial protocol	SE HU SK CZ BG
Global end of trial date	07 February 2022

Results information

Result version number	v1 (current)
This version publication date	22 February 2023
First version publication date	22 February 2023

Trial information

Trial identification

Sponsor protocol code	B7921023
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04413617
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 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	23 December 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of each of 2 combinations (PF-06650833 [zimlovisertib]+ PF-06651600 [ritlecinib] and PF-06650833 [zimlovisertib]+ tofacitinib) individually to tofacitinib alone at Week 12 in participants with moderately - severely active rheumatoid arthritis (RA) who had an inadequate response to methotrexate.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 32
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Chile: 42
Country: Number of subjects enrolled	Czechia: 72
Country: Number of subjects enrolled	Georgia: 28
Country: Number of subjects enrolled	Hungary: 42
Country: Number of subjects enrolled	Poland: 128
Country: Number of subjects enrolled	Slovakia: 20
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Ukraine: 68
Worldwide total number of subjects	460
EEA total number of subjects	319

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	403
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with moderately to severely active RA were enrolled. Up to 25% of subjects were permitted to have a prior history of exposure to 1 and only 1 blocker of tumor necrosis factor (TNF) alpha; no other prior biologic disease modifying antirheumatic drug or Janus kinase inhibitor exposure was permitted.

Pre-assignment

Screening details:

A total of 626 subjects were screened, of which 460 subjects were randomized to treatment and received at least 1 dose of study intervention.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib 11mg MR

Arm description:

Subjects received tofacitinib 11mg as modified release (MR) tablets once daily (QD).

Arm type	Active comparator
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tofacitinib 11mg as MR tablets QD.

Arm title	PF-06651600 100mg
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Arm description:

Subjects received PF-06651600 100mg tablets QD.

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

Dosage and administration details:

Subjects received PF-06651600 50mg*2 tablets QD.

Arm title	PF-06650833 400mg MR
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Arm description:

Subjects received PF-06650833 400mg as MR tablets QD.

Arm type	Experimental
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Investigational medicinal product name	PF-06650833
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use
Dosage and administration details:	
Subjects received PF-06650833 200mg*2 as MR tablets QD.	
Arm title	PF-06650833 400mg MR + tofacitinib 11mg MR

Arm description:

Subjects received PF-06650833 400mg MR tablets coadministered with tofacitinib 11mg MR tablets QD.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received PF-06650833 200*2mg MR tablets coadministered with tofacitinib 11mg MR tablets QD.

Investigational medicinal product name	PF-06650833
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received PF-06650833 200mg*2 MR tablets coadministered with tofacitinib 11mg MR tablets QD.

Arm title	PF-06650833 400mg MR + PF-06651600 100mg
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Arm description:

Subjects received PF-06650833 400mg MR tablets coadministered with PF-06651600 100mg tablets QD.

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

Dosage and administration details:

Subjects received PF-06650833 200mg*2 MR tablets coadministered with PF-06651600 50mg*2 tablets QD.

Investigational medicinal product name	PF-06650833
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received PF-06650833 200mg*2 MR tablets coadministered with PF-06651600 50mg*2 tablets QD.

Number of subjects in period 1	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR
Started	102	77	77
Completed	95	71	73
Not completed	7	6	4
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	3	4	2
Adverse event, non-fatal	1	-	-
COVID-19	-	1	-
Lack of efficacy	2	-	2
Protocol deviation	-	1	-
Refused to come for FU visit	-	-	-

Number of subjects in period 1	PF-06650833 400mg MR + tofacitinib 11mg MR	PF-06650833 400mg MR + PF-06651600 100mg
Started	103	101
Completed	95	96
Not completed	8	5
Adverse event, serious fatal	-	-
Consent withdrawn by subject	5	3
Adverse event, non-fatal	1	1
COVID-19	-	-
Lack of efficacy	1	-
Protocol deviation	-	1
Refused to come for FU visit	1	-

Baseline characteristics

Reporting groups

Reporting group title	Tofacitinib 11mg MR
Reporting group description:	
Subjects received tofacitinib 11mg as modified release (MR) tablets once daily (QD).	
Reporting group title	PF-06651600 100mg
Reporting group description:	
Subjects received PF-06651600 100mg tablets QD.	
Reporting group title	PF-06650833 400mg MR
Reporting group description:	
Subjects received PF-06650833 400mg as MR tablets QD.	
Reporting group title	PF-06650833 400mg MR + tofacitinib 11mg MR
Reporting group description:	
Subjects received PF-06650833 400mg MR tablets coadministered with tofacitinib 11mg MR tablets QD.	
Reporting group title	PF-06650833 400mg MR + PF-06651600 100mg
Reporting group description:	
Subjects received PF-06650833 400mg MR tablets coadministered with PF-06651600 100mg tablets QD.	

Reporting group values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR
Number of subjects	102	77	77
Age Categorical			
Units: Subjects			
18-44	25	17	11
45-64	68	49	56
>=65	9	11	10
Age Continuous			
Units: Years			
arithmetic mean	51.2	52.8	53.6
standard deviation	± 10.63	± 10.90	± 9.87
Sex: Female, Male			
Units: Subjects			
Female	82	62	61
Male	20	15	16
Race/Ethnicity, Customized			
Units: Subjects			
White	101	76	77
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Multiracial	0	1	0

Reporting group values	PF-06650833 400mg MR + tofacitinib 11mg MR	PF-06650833 400mg MR + PF-06651600 100mg	Total
Number of subjects	103	101	460
Age Categorical			
Units: Subjects			
18-44	19	21	93
45-64	71	66	310

>=65	13	14	57
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Age Continuous Units: Years arithmetic mean standard deviation	54.0 ± 10.41	53.0 ± 10.40	-
Sex: Female, Male Units: Subjects			
Female	78	73	356
Male	25	28	104
Race/Ethnicity, Customized Units: Subjects			
White	102	101	457
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	1	0	1
Multiracial	0	0	1

End points

End points reporting groups

Reporting group title	Tofacitinib 11mg MR
Reporting group description: Subjects received tofacitinib 11mg as modified release (MR) tablets once daily (QD).	
Reporting group title	PF-06651600 100mg
Reporting group description: Subjects received PF-06651600 100mg tablets QD.	
Reporting group title	PF-06650833 400mg MR
Reporting group description: Subjects received PF-06650833 400mg as MR tablets QD.	
Reporting group title	PF-06650833 400mg MR + tofacitinib 11mg MR
Reporting group description: Subjects received PF-06650833 400mg MR tablets coadministered with tofacitinib 11mg MR tablets QD.	
Reporting group title	PF-06650833 400mg MR + PF-06651600 100mg
Reporting group description: Subjects received PF-06650833 400mg MR tablets coadministered with PF-06651600 100mg tablets QD.	

Primary: Change from baseline (BL) in Disease Activity Score (DAS)28-C Reactive protein (CRP) at Week 12

End point title	Change from baseline (BL) in Disease Activity Score (DAS)28-C Reactive protein (CRP) at Week 12
End point description: DAS28 is a measure based on assessment of 28 joints for tenderness and swelling (tender and swollen joint counts). DAS28-CRP is derived using differential weighting given to 4 components: tender joint count (range: 0-28), swollen joint count (range: 0-28), patient global assessment (recorded on a visual analog scale [VAS] scale of 0-100 mm), and CRP (milligram per liter). The lower the DAS28-CRP score is, the better the participant has response (remission = score < 2.6, low disease activity = score ≤ 3.2). Modified Intent to Treat (mITT) data set is used, which included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects were analyzed according to the randomized intervention. Subjects with non-missing data at a given visit were included.	
End point type	Primary
End point timeframe: BL (defined as the last non-missing measurement collected prior to the first administration of study drug on Day 1), Week 12	

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	69	71	96
Units: Units on a scale				
least squares mean (confidence interval 90%)	-2.30 (-2.49 to -2.11)	-2.20 (-2.43 to -1.98)	-1.82 (-2.04 to -1.60)	-2.65 (-2.84 to -2.46)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: Units on a scale				
least squares mean (confidence interval 90%)	-2.35 (-2.54 to -2.15)			

Statistical analyses

Statistical analysis title	Comparison for DAS28-CRP
Statistical analysis description:	
The primary clinical hypothesis is that mean decrease at Week 12 in DAS28-CRP score in one or both combo arms exceeds the mean decrease in the reference (tofacitinib) treatment arm, regardless of occurrence of intercurrent events. The null hypothesis is that the mean decrease in DAS28-CRP score at Week 12 is identical in the control (tofacitinib arm) and combination arms.	
Comparison groups	PF-06650833 400mg MR + tofacitinib 11mg MR v Tofacitinib 11mg MR
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.0158
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.62
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.163

Notes:

[1] - Mixed Model Repeated Measures used the change from BL value of DAS28-CRP as an outcome and treatment, scheduled study visit, BL value of DAS28-CRP, treatment by visit interaction and BL by visit interaction as fixed effects. The model used the unstructured covariance matrix.

Statistical analysis title	Comparison for DAS28-CRP
Statistical analysis description:	
The primary clinical hypothesis is that mean decrease at Week 12 in DAS28-CRP score in one or both combo arms exceeds the mean decrease in the reference (tofacitinib) treatment arm, regardless of occurrence of intercurrent events. The null hypothesis is that the mean decrease in DAS28-CRP score at Week 12 is identical in the control (tofacitinib arm) and combination arms.	
Comparison groups	PF-06650833 400mg MR + PF-06651600 100mg v Tofacitinib 11mg MR
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.3933
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (final values)
Point estimate	-0.04

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.32
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.164

Notes:

[2] - Mixed Model Repeated Measures used the change from BL value of DAS28-CRP as an outcome and treatment, scheduled study visit, BL value of DAS28-CRP, treatment by visit interaction and BL by visit interaction as fixed effects. The model used the unstructured covariance matrix.

Secondary: DAS28-CRP remission (<2.6) rates at Week 24

End point title	DAS28-CRP remission (<2.6) rates at Week 24
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End point description:

DAS28-CRP is derived using differential weighting given to 4 components: tender joint count, swollen joint count, patient global assessment, and CRP. Remission is defined as DAS28-CRP score <2.6. Remission rate = the number of responders (who had remission) / (number of responders + non-responders + non-responder assigned by non-responder imputation [NRI] after removal of missingness due to COVID-19 and missing components at a given visit). The NRI data set included responders, non-responders, and non-responder assigned by NRI after removal of missingness due to COVID-19 and missing components at a given visit.

End point type	Secondary
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End point timeframe:

Week 24

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	76	76	103
Units: Percentage of subjects				
number (confidence interval 90%)	24.0 (17.1 to 31.8)	22.4 (14.8 to 31.3)	11.8 (6.7 to 19.3)	40.8 (32.6 to 48.7)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: Percentage of subjects				
number (confidence interval 90%)	31.3 (24.1 to 39.8)			

Statistical analyses

Secondary: Number of subjects with treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs), and discontinuation (DC) due to TEAEs

End point title	Number of subjects with treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs), and discontinuation (DC) due to TEAEs
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End point description:

An adverse event (AE) was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A serious AE (SAE) was any untoward medical occurrence that: resulted in death; was life-threatening; required inpatient hospitalization/prolongation of hospitalization; resulted in persistent disability/incapacity; was a congenital anomaly/birth defect; or other serious situations. TEAEs were events between first dose of study drug and up to FU visit that were absent before treatment or worsened after treatment. AEs presented below were TEAEs. The investigator was required to use clinical judgment to assess the potential relationship between investigational product and each AE, to define an treatment-related AE. The safety analysis set is used, which included all participants randomly assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From first dose of study intervention (Day 1) to Week 28

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	77	77	103
Units: Subjects				
All-causality TEAEs	60	42	38	51
Treatment-related TEAEs	15	17	13	20
All-causality TESAEs	3	3	3	0
Treatment-related TESAEs	0	0	0	0
DC from study due to all-causality AEs	2	0	0	1
DC from study due to treatment-related AEs	1	0	0	1
Study drug withdrawal due to all-causality AEs	0	6	6	4
Study drug withdrawal due to treatment-related AEs	0	4	4	3

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
All-causality TEAEs	55			
Treatment-related TEAEs	25			
All-causality TESAEs	1			

Treatment-related TESAEs	0			
DC from study due to all-causality AEs	1			
DC from study due to treatment-related AEs	0			
Study drug withdrawal due to all-causality AEs	6			
Study drug withdrawal due to treatment-related AEs	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinical laboratory abnormalities (hematology and chemistry, without regard to baseline abnormality)

End point title	Number of subjects with clinical laboratory abnormalities (hematology and chemistry, without regard to baseline abnormality)
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End point description:

Clinical laboratory abnormality was determined at the investigator's discretion. The analysis set included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects with evaluable laboratory values were analyzed. Due to system limitation, for some lab parameters, the actual number of subjects analyzed were not 101, 77, 77, 101, 101 and were denoted in the paramter.

End point type	Secondary
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End point timeframe:

From BL to Week 28

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	77	77	101
Units: Subjects				
Hemoglobin<0.8xLLN	2	2	0	2
Erythrocytes<0.8xLLN	0	2	0	0
Ery. Mean Corpuscular Volume <0.9xLLN	3	2	0	2
Ery. Mean Corpuscular Volume >1.1xULN	4	3	4	3
Ery. Mean Corpuscular HGB<0.9xLLN	8	5	3	7
Ery. Mean Corpuscular HGB Conc. <0.9xLLN	8	6	12	10
Platelets>1.75xULN	0	0	0	1
Reticulocytes/Erythrocytes>1.5xULN	2	1	2	1
Leukocytes<0.6xLLN	0	1	0	0
Leukocytes>1.5xULN	2	2	1	1
Lymphocytes<0.8xLLN	7	16	3	6
Lymphocytes>1.2xULN	3	2	1	1
Lymphocytes/Leukocytes<0.8xLLN	6	11	9	6

Lymphocytes/Leukocytes>1.2xULN	1	1	1	5
Neutrophils<0.8xLLN	2	2	3	5
Neutrophils>1.2xULN	11	16	8	5
Neutrophils/Leukocytes<0.8xLLN	1	0	0	2
Neutrophils/Leukocytes>1.2xULN	5	9	6	3
Basophils>1.2xULN	0	0	1	1
Eosinophils>1.2xULN	0	0	3	1
Eosinophils/Leukocytes>1.2xULN	1	0	5	4
Monocytes>1.2xULN	2	1	1	0
Monocytes/Leukocytes>1.2xULN	8	12	6	11
Activated PTT>1.1xULN (n=101,77,77,102,101)	9	9	9	10
Prothrombin Time>1.1xULN (n=101,77,77,102,101)	7	6	6	2
ESR>1.5xULN (n=101,77,77,102,101)	72	59	58	71
Bilirubin>1.5xULN (n=101,77,77,102,101)	2	0	0	0
AST>3.0xULN (n=101,77,77,102,101)	0	0	2	1
ALT>3.0xULN (n=101,77,77,102,101)	0	1	7	2
Urea Nitrogen>1.3xULN (n=101,77,77,102,101)	4	1	5	4
Creatinine >1.3xULN (n=101,77,77,102,101)	0	0	0	1
Urate>1.2xULN (n=101,77,77,102,101)	3	2	2	4
Cholesterol>1.3xULN (n=94,71,73,100,91)	22	13	10	24
HDL Cholesterol <0.8xLLN (n=94,70,69,98,90)	1	3	1	0
LDL Cholesterol>1.2xULN (n=92,70,68,98,88)	9	5	1	5
Sodium<0.95xLLN (n=101,77,77,102,101)	0	1	0	0
Potassium<0.9xLLN (n=101,77,77,102,101)	0	1	2	0
Potassium>1.1xULN (n=101,77,77,102,101)	2	3	0	1
Chloride<0.9xLLN (n=101,77,77,102,101)	0	1	0	0
Calcium<0.9xLLN (n=101,77,77,102,101)	0	0	0	0
Bicarbonate<0.9xLLN (n=101,77,77,102,101)	4	2	0	3
Creatine Kinase>2.0xULN (n=101,77,77,102,101)	4	7	1	10
Troponin I>1.0xULN (n=101,77,77,102,101)	2	3	2	4
Glucose-FASTING>1.5xULN (n=101,77,77,102,101)	3	5	10	10
Triglycerides-FASTING>1.3xULN (n=94,71,73,100,91)	9	7	4	7
Apolipoprotein A1>1.5xULN (n=93,68,66,93,87)	0	1	0	0
Apolipoprotein B>1.5xULN (n=93,68,66,93,87)	0	1	0	0

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
Hemoglobin<0.8xLLN	2			
Erythrocytes<0.8xLLN	0			
Ery. Mean Corpuscular Volume <0.9xLLN	0			
Ery. Mean Corpuscular Volume >1.1xULN	4			
Ery. Mean Corpuscular HGB<0.9xLLN	4			
Ery. Mean Corpuscular HGB Conc. <0.9xLLN	4			
Platelets>1.75xULN	0			
Reticulocytes/Erythrocytes>1.5xULN	1			
Leukocytes<0.6xLLN	1			
Leukocytes>1.5xULN	3			
Lymphocytes<0.8xLLN	13			
Lymphocytes>1.2xULN	2			
Lymphocytes/Leukocytes<0.8xLLN	10			
Lymphocytes/Leukocytes>1.2xULN	3			
Neutrophils<0.8xLLN	4			
Neutrophils>1.2xULN	14			
Neutrophils/Leukocytes<0.8xLLN	1			
Neutrophils/Leukocytes>1.2xULN	7			
Basophils>1.2xULN	0			
Eosinophils>1.2xULN	0			
Eosinophils/Leukocytes>1.2xULN	1			
Monocytes>1.2xULN	2			
Monocytes/Leukocytes>1.2xULN	17			
Activated PTT>1.1xULN (n=101,77,77,102,101)	10			
Prothrombin Time>1.1xULN (n=101,77,77,102,101)	9			
ESR>1.5xULN (n=101,77,77,102,101)	63			
Bilirubin>1.5xULN (n=101,77,77,102,101)	0			
AST>3.0xULN (n=101,77,77,102,101)	0			
ALT>3.0xULN (n=101,77,77,102,101)	0			
Urea Nitrogen>1.3xULN (n=101,77,77,102,101)	2			
Creatinine >1.3xULN (n=101,77,77,102,101)	0			
Urate>1.2xULN (n=101,77,77,102,101)	1			
Cholesterol>1.3xULN (n=94,71,73,100,91)	20			
HDL Cholesterol <0.8xLLN (n=94,70,69,98,90)	1			
LDL Cholesterol>1.2xULN (n=92,70,68,98,88)	8			
Sodium<0.95xLLN (n=101,77,77,102,101)	0			
Potassium<0.9xLLN (n=101,77,77,102,101)	1			

Potassium>1.1xULN (n=101,77,77,102,101)	1			
Chloride<0.9xLLN (n=101,77,77,102,101)	0			
Calcium<0.9xLLN (n=101,77,77,102,101)	1			
Bicarbonate<0.9xLLN (n=101,77,77,102,101)	2			
Creatine Kinase>2.0xULN (n=101,77,77,102,101)	9			
Troponin I>1.0xULN (n=101,77,77,102,101)	4			
Glucose-FASTING>1.5xULN (n=101,77,77,102,101)	2			
Triglycerides-FASTING>1.3xULN (n=94,71,73,100,91)	5			
Apolipoprotein A1>1.5xULN (n=93,68,66,93,87)	0			
Apolipoprotein B>1.5xULN (n=93,68,66,93,87)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with change from baseline in vital signs data meeting the pre-defined categorical summarization criteria

End point title	Number of subjects with change from baseline in vital signs data meeting the pre-defined categorical summarization criteria
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End point description:

Abnormality in change from BL in vital signs included: sitting/semi-supine diastolic blood pressure (BP) increase and decrease from BL of ≥ 20 mmHg, systolic BP increase and decrease from BL of ≥ 30 mmHg. The safety analysis set is used, which included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects with evaluable vital signs data were analyzed.

End point type	Secondary
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End point timeframe:

From BL to Week 28

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	77	77	102
Units: Subjects				
Diastolic BP increase ≥ 20 mmHg	1	2	3	6
Diastolic BP decrease ≥ 20 mmHg	0	0	0	0
Systolic BP increase ≥ 30 mmHg	1	3	4	2
Systolic BP decrease ≥ 30 mmHg	0	0	0	0

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
Diastolic BP increase ≥ 20 mmHg	3			
Diastolic BP decrease ≥ 20 mmHg	0			
Systolic BP increase ≥ 30 mmHg	3			
Systolic BP decrease ≥ 30 mmHg	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events of special interest

End point title	Number of subjects with adverse events of special interest
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End point description:

These AEs included severe and opportunistic infection AEs; herpes virus infection AEs; clinically significant categorical increases in hepatic enzymes AST, and ALT and total bilirubin, and potential cases meeting Hy's Law criteria for increased risk of drug induced liver injury (DILI); major adverse cardiovascular events, including pulmonary embolism and deep vein thrombosis, cerebrovascular accident ; AEs for decreased renal function, acute kidney injury, clinically significant increases in serum creatinine (Scr) and decreases in estimated glomerular filtration rate (eGFR). Only subjects with AEs mentioned above were reported. The safety analysis set is used, which included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

From first dose of study intervention (Day 1) to Week 28

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	77	77	103
Units: Subjects				
Herpes Zoster	1	1	0	2
Oral Herpes	1	0	0	1
ALT Increased	0	0	3	2
AST Increased	0	0	2	2
Hyperbilirubinaemia	1	0	0	0
Transaminases Increased	0	0	1	0
Hepatic Enzyme Increased	0	0	1	0
Liver Injury	0	0	1	0

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
Herpes Zoster	0			
Oral Herpes	2			
ALT Increased	0			
AST Increased	0			
Hyperbilirubinaemia	0			
Transaminases Increased	0			
Hepatic Enzyme Increased	0			
Liver Injury	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in DAS28-CRP at Week 24

End point title	Change from baseline in DAS28-CRP at Week 24
End point description:	
<p>DAS28 is a measure based on assessment of 28 joints for tenderness and swelling (tender and swollen joint counts). DAS28-CRP is derived using differential weighting given to 4 components: tender joint count (range: 0-28), swollen joint count (range: 0-28), patient global assessment (recorded on a visual analog scale [VAS] scale of 0-100 mm), and CRP (milligram per liter). The lower the DAS28-CRP score is, the better the participant has response (remission = score<2.6, low disease activity = score≤3.2). mITT data set is used, which included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects were analyzed according to the randomized intervention. Subjects with non-missing data at a given visit were included.</p>	
End point type	Secondary
End point timeframe:	
BL (defined as the last non-missing measurement collected prior to the first administration of study drug on Day 1), Week 24	

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	54	49	84
Units: Units on a scale				
least squares mean (confidence interval 90%)	-2.66 (-2.88 to -2.45)	-2.53 (-2.78 to -2.28)	-2.26 (-2.51 to -2.00)	-3.05 (-3.26 to -2.85)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: Units on a scale				
least squares mean (confidence interval 90%)	-2.87 (-3.08 to -2.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: American College of Rheumatology (ACR)20, ACR 50, ACR 70, and ACR 90 responder rates at Week 12 and Week 24

End point title	American College of Rheumatology (ACR)20, ACR 50, ACR 70, and ACR 90 responder rates at Week 12 and Week 24
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End point description:

The American College of Rheumatology's definition for calculating improvement in rheumatoid arthritis (ACR20) is calculated as a $\geq 20\%$ improvement in tender and swollen joint counts and 20% improvement in 3 of the 5 remaining ACR core set measures: patient and physician global assessments, pain, disability, and CRP. Similarly, ACR50, ACR70, and ACR 90 were calculated with the respective percent improvement. Responder rate = number of responders (who had ACR20/50/70/90 response)/(number of responders + non-responders + non-responder assigned by NRI after removal of missingness due to COVID-19 and missing components at a given visit). NRI data set is used, which included responders, non-responders, and non-responder assigned by NRI after removal of missingness due to COVID-19 and missing components at a given visit. Due to system limit, the actual number of subjects analyzed for each parameter is denoted beside the parameter.

End point type	Secondary
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End point timeframe:

BL (defined as the last non-missing measurement collected prior to the first administration of study drug on Day 1), Week 12, Week 24

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	77	77	103
Units: Percentage of subjects				
number (confidence interval 90%)				
ACR20 (Week 12) (n =103,101,101,77,76)	83.17 (75.94 to 88.98)	72.73 (63.80 to 80.94)	75.00 (66.26 to 82.24)	86.41 (79.94 to 91.59)
ACR50 (Week 12) (n=102,101,101,77,76)	46.53 (38.04 to 55.19)	44.16 (34.59 to 54.16)	38.16 (29.16 to 47.81)	62.75 (54.69 to 70.75)
ACR70 (Week 12) (n=103,101,101,77,76)	23.76 (16.96 to 31.42)	18.18 (11.34 to 26.08)	10.53 (5.39 to 18.17)	21.36 (15.35 to 28.95)

ACR90 (Week 12) (n=103,101,101,77,76)	0.99 (0.10 to 4.12)	1.30 (0.14 to 5.32)	1.32 (0.14 to 5.39)	2.91 (1.07 to 6.86)
ACR20 (Week 24) (n=103,100,101,77,76)	75.25 (67.64 to 82.11)	67.53 (57.99 to 76.32)	55.26 (45.20 to 65.01)	75.73 (68.31 to 82.41)
ACR50 (Week 24) (n=103,100,101,77,76)	65.35 (57.14 to 73.21)	54.55 (44.56 to 63.80)	43.42 (33.74 to 53.50)	65.05 (57.08 to 72.34)
ACR70 (Week 24) (n=103,100,101,77,76)	44.55 (36.60 to 53.22)	31.17 (22.51 to 40.74)	27.63 (19.32 to 36.52)	45.63 (37.25 to 54.20)
ACR90 (Week 24) (n=103,100,101,77,76)	9.90 (5.58 to 16.09)	5.19 (2.28 to 11.34)	1.32 (0.14 to 5.39)	12.62 (8.05 to 19.19)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage of subjects				
number (confidence interval 90%)				
ACR20 (Week 12) (n =103,101,101,77,76)	79.21 (71.99 to 85.62)			
ACR50 (Week 12) (n=102,101,101,77,76)	54.46 (45.79 to 62.57)			
ACR70 (Week 12) (n=103,101,101,77,76)	25.74 (19.17 to 33.29)			
ACR90 (Week 12) (n=103,101,101,77,76)	3.96 (1.74 to 8.58)			
ACR20 (Week 24) (n=103,100,101,77,76)	70.00 (61.87 to 77.31)			
ACR50 (Week 24) (n=103,100,101,77,76)	65.00 (56.68 to 72.92)			
ACR70 (Week 24) (n=103,100,101,77,76)	44.00 (35.61 to 52.72)			
ACR90 (Week 24) (n=103,100,101,77,76)	18.00 (12.27 to 25.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the Tender/Painful and Swollen Joint Count at Week 12 and Week 24

End point title	Change from baseline in the Tender/Painful and Swollen Joint Count at Week 12 and Week 24
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End point description:

Tender/Painful Joint Count 68 (TJC68) was assessed by a blinded joint assessor to determine the number of joints considered tender/painful in upper body, upper/lower extremity. The response to pressure/motion on each joint was assessed using: Present/Absent/Not Done/Not Applicable (for artificial/missing joints). The 28-joints set is the subset of 68 joints set including the following joints: shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints and knees. TJC28 was calculated by Pfizer from TJC68. Higher scores indicate higher level of disability. mITT data set is used, including all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects with non-missing data at a given visit were included and were analyzed according to the randomized intervention. Due to system limit, the actual number of subjects analyzed for each paramter was denoted beside the parmater.

End point type	Secondary
End point timeframe:	
BL (defined as the last non-missing measurement collected prior to the first administration of study drug on Day 1), Week 12, Week 24	

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	77	77	103
Units: Joints				
least squares mean (confidence interval 90%)				
TJC28 (Week 12) (n=100,93,96,69,72)	-9.84 (-10.63 to -9.05)	-9.83 (-10.76 to -8.91)	-8.82 (-9.73 to -7.92)	-9.87 (-10.65 to -9.09)
TJC68 (Week 12) (n=100,93,96,69,72)	-15.32 (-16.47 to -14.18)	-14.80 (-16.13 to -13.46)	-13.76 (-15.07 to -12.46)	-14.96 (-16.09 to -13.83)
SJC28 (Week 12) (n=100,93,96,69,72)	-7.86 (-8.41 to -7.30)	-8.30 (-8.95 to -7.65)	-7.80 (-8.44 to -7.15)	-8.61 (-9.16 to -8.06)
SJC66 (Week 12) (n=100,93,96,69,72)	-10.34 (-11.05 to -9.63)	-10.75 (-11.58 to -9.92)	-10.18 (-11.00 to -9.37)	-11.29 (-11.99 to -10.59)
TJC28 (Week 24) (n=84,74,81,55,49)	-10.60 (-11.34 to -9.86)	-10.47 (-11.34 to -9.59)	-10.31 (-11.20 to -9.42)	-11.33 (-12.06 to -10.61)
TJC68 (Week 24) (n=84,74,81,55,49)	-16.76 (-17.88 to -15.64)	-16.69 (-18.02 to -15.36)	-15.79 (-17.13 to -14.46)	-16.68 (-17.78 to -15.57)
SJC28 (Week 24) (n=84,74,81,55,49)	-8.76 (-9.29 to -8.24)	-8.71 (-9.33 to -8.08)	-8.28 (-8.92 to -7.65)	-8.83 (-9.34 to -8.31)
SJC66 (Week 24) (n=84,74,81,55,49)	-11.59 (-12.21 to -10.97)	-11.45 (-12.19 to -10.71)	-11.10 (-11.86 to -10.34)	-11.41 (-12.02 to -10.80)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Joints				
least squares mean (confidence interval 90%)				
TJC28 (Week 12) (n=100,93,96,69,72)	-9.78 (-10.58 to -8.98)			
TJC68 (Week 12) (n=100,93,96,69,72)	-15.66 (-16.81 to -14.50)			
SJC28 (Week 12) (n=100,93,96,69,72)	-8.16 (-8.73 to -7.60)			
SJC66 (Week 12) (n=100,93,96,69,72)	-10.90 (-11.62 to -10.19)			
TJC28 (Week 24) (n=84,74,81,55,49)	-11.44 (-12.20 to -10.68)			
TJC68 (Week 24) (n=84,74,81,55,49)	-17.68 (-18.82 to -16.53)			
SJC28 (Week 24) (n=84,74,81,55,49)	-9.44 (-9.98 to -8.90)			

SJC66 (Week 24) (n=84,74,81,55,49)	-12.38 (-13.03 to -11.74)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the Physician's Global Assessment (PhGA) of Arthritis at Week 12 and Week 24

End point title	Change from baseline in the Physician's Global Assessment (PhGA) of Arthritis at Week 12 and Week 24
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End point description:

PhGA of Arthritis is an evaluation done by investigator based on the subject's disease signs, functional capacity and physical examination, and should be independent of the Patient's Global Assessment of Arthritis. The investigator's response was recorded using a 100 mm visual analog scale (VAS). Higher scores indicate higher level of disability. mITT data set is used, which included all subjects randomly assigned to study intervention and who took at least 1 dose of study intervention. Subjects were analyzed according to the randomized intervention. Subjects with non-missing data at a given visit were included. Due to system limit, the actual number of subjects analyzed for each parameter is denoted beside the parameter.

End point type	Secondary
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End point timeframe:

BL (defined as the last non-missing measurement collected prior to the first administration of study drug on Day 1), Week 12, Week 24

End point values	Tofacitinib 11mg MR	PF-06651600 100mg	PF-06650833 400mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	77	77	103
Units: Units on a scale				
least squares mean (confidence interval 90%)				
PhGA of Arthritis (Week 12) (n=100,93,96,69,72)	-40.86 (-43.72 to -38.00)	-38.62 (-41.95 to -35.28)	-31.56 (-34.82 to -28.30)	-43.50 (-46.32 to -40.69)
PhGA of Arthritis (Week 24) (n=84,74,81,55,49)	-47.31 (-49.98 to -44.63)	-43.42 (-46.60 to -40.25)	-39.27 (-42.49 to -36.05)	-47.50 (-50.13 to -44.87)

End point values	PF-06650833 400mg MR + PF-06651600 100mg			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Units on a scale				
least squares mean (confidence interval 90%)				

PhGA of Arthritis (Week 12) (n=100,93,96,69,72)	-41.20 (-44.06 to -38.34)			
PhGA of Arthritis (Week 24) (n=84,74,81,55,49)	-48.21 (-50.95 to -45.47)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study intervention (Day 1) to Week 28

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	PF-06651600 100mg
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Reporting group description:

Subjects received PF-06651600 100mg tablets QD.

Reporting group title	Tofacitinib 11mg MR
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Reporting group description:

Subjects received tofacitinib 11mg MR tablets QD.

Reporting group title	PF-06650833 400mg MR + tofacitinib 11mg MR
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Reporting group description:

Subjects received PF-06650833 400mg MR tablets coadministered with tofacitinib 11mg MR tablets QD.

Reporting group title	PF-06650833 400mg MR + PF-06651600 100mg
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Reporting group description:

Subjects received PF-06650833 400mg MR tablets coadministered with PF-06651600 100mg tablets QD.

Reporting group title	PF-06650833 400mg MR
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Reporting group description:

Subjects received PF-06650833 400mg MR tablets QD.

Serious adverse events	PF-06651600 100mg	Tofacitinib 11mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 77 (3.90%)	3 / 102 (2.94%)	0 / 103 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin squamous cell carcinoma recurrent			
subjects affected / exposed	0 / 77 (0.00%)	1 / 102 (0.98%)	0 / 103 (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
Uterine leiomyoma			

subjects affected / exposed	1 / 77 (1.30%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 77 (1.30%)	0 / 102 (0.00%)	0 / 103 (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
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 102 (0.00%)	0 / 103 (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
Uterine polyp			
subjects affected / exposed	0 / 77 (0.00%)	0 / 102 (0.00%)	0 / 103 (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
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 77 (0.00%)	0 / 102 (0.00%)	0 / 103 (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
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 77 (0.00%)	0 / 102 (0.00%)	0 / 103 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 77 (0.00%)	0 / 102 (0.00%)	0 / 103 (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
Coronavirus infection			

subjects affected / exposed	0 / 77 (0.00%)	1 / 102 (0.98%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 77 (1.30%)	0 / 102 (0.00%)	0 / 103 (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

Serious adverse events	PF-06650833 400mg MR + PF- 06651600 100mg	PF-06650833 400mg MR	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 101 (0.99%)	3 / 77 (3.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin squamous cell carcinoma recurrent			
subjects affected / exposed	0 / 101 (0.00%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 101 (0.00%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 101 (0.00%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine polyp			
subjects affected / exposed	0 / 101 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 101 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PF-06651600 100mg	Tofacitinib 11mg MR	PF-06650833 400mg MR + tofacitinib 11mg MR
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 77 (23.38%)	24 / 102 (23.53%)	19 / 103 (18.45%)

Investigations SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	1 / 77 (1.30%) 1	7 / 102 (6.86%) 7	4 / 103 (3.88%) 4
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 77 (5.19%) 4	4 / 102 (3.92%) 4	3 / 103 (2.91%) 3
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	5 / 77 (6.49%) 5	4 / 102 (3.92%) 4	1 / 103 (0.97%) 3
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Rheumatoid arthritis subjects affected / exposed occurrences (all)	5 / 77 (6.49%) 5 4 / 77 (5.19%) 4	3 / 102 (2.94%) 3 3 / 102 (2.94%) 3	2 / 103 (1.94%) 2 1 / 103 (0.97%) 1
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	2 / 77 (2.60%) 2 1 / 77 (1.30%) 1	3 / 102 (2.94%) 4 5 / 102 (4.90%) 7	3 / 103 (2.91%) 3 7 / 103 (6.80%) 9

Non-serious adverse events	PF-06650833 400mg MR + PF- 06651600 100mg	PF-06650833 400mg MR	
Total subjects affected by non-serious adverse events subjects affected / exposed	26 / 101 (25.74%)	11 / 77 (14.29%)	
Investigations SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	8 / 101 (7.92%) 8	2 / 77 (2.60%) 2	
Nervous system disorders Headache			

subjects affected / exposed occurrences (all)	7 / 101 (6.93%) 7	2 / 77 (2.60%) 3	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	3 / 101 (2.97%) 3	2 / 77 (2.60%) 2	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Rheumatoid arthritis subjects affected / exposed occurrences (all)	2 / 101 (1.98%) 2 1 / 101 (0.99%) 1	1 / 77 (1.30%) 1 4 / 77 (5.19%) 4	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	6 / 101 (5.94%) 6 3 / 101 (2.97%) 3	1 / 77 (1.30%) 1 1 / 77 (1.30%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported