Clinical trial results:
A Randomized Comparative Study Assessing the Switching Between PF-06410293 And Humira® In Combination With Methotrexate In Participants With Moderately To Severely Active Rheumatoid Arthritis

Summary

EudraCT number	2019-000284-24
Trial protocol	CZ LT
Global end of trial date	22 June 2021

Results information

Result version number	v2 (current)
This version publication date	11 February 2024
First version publication date	03 July 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	B5381012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04230213
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate interchangeability of PF-06510293 and Humira by examining adalimumab steady-state pharmacokinetics in a switching arm (following 3 switches between Humira and PF-06410293) as compared to a non-switching arm (receiving only Humira).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bosnia and Herzegovina: 35
Country: Number of subjects enrolled	Bulgaria: 28
Country: Number of subjects enrolled	Czechia: 69
Country: Number of subjects enrolled	Lithuania: 13
Country: Number of subjects enrolled	Poland: 119
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	Serbia: 37
Country: Number of subjects enrolled	South Africa: 21
Country: Number of subjects enrolled	Ukraine: 55
Country: Number of subjects enrolled	United States: 22
Worldwide total number of subjects	445
EEA total number of subjects	229

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)	369
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 455 subjects were enrolled in the study, of which 10 subjects were excluded from all the data analyses due to violation of GCP principles. Thus, these 10 subjects were not included in any section of results.

Period 1

Period 1 title	TP1: Week 0 (Day 1) to Week 10
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Humira (Adalimumab)

Arm description:

All subjects received Humira 40 milligrams (mg) once every 2 weeks subcutaneously for 10 weeks during Treatment Period 1 (TP1).

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Adalimumab 40 mg, single subcutaneous injection in abdomen or upper front of either thigh every 2 weeks for 10 weeks.

Number of subjects in period 1	Humira (Adalimumab)
Started	445
Completed	427
Not completed	18
Consent withdrawn by subject	7
Physician decision	3
Unspecified	8

Period 2

Period 2 title	TP2 up to End of Study:Week 10 to 36
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Switching Arm: Humira and PF-06410293 (Adalimumab)

Arm description:

Subjects after completing TP1, were randomised to receive PF-06410293 40 mg once every 2 weeks subcutaneously for 6 weeks during Treatment Period 2 (TP2). TP2 was followed by Treatment Period 3 (TP3). In TP3 subjects received Humira 40 mg once every 2 weeks subcutaneously for another 6 weeks. TP3 was followed by Treatment Period 4 (TP4). In TP4 subjects received PF-06410293 40 mg once every 2 weeks subcutaneously for next 10 weeks. Subjects were followed for 4 weeks post last dose.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira 40 mg, single subcutaneous injection in abdomen or upper front of either thigh every 2 weeks for 6 weeks during TP3.

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	PF-06410293
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06410293 40 mg, single subcutaneous injection in abdomen or upper front of either thigh once every 2 weeks for 6 weeks during TP2 and for 10 weeks during TP4.

Arm title	Non-switching Arm: Humira (Adalimumab)

Arm description:

Subjects after completing TP1, were randomised to continue treatment with Humira 40 mg once every 2 weeks subcutaneously for 22 weeks. Subjects were followed for 4 weeks post last dose.

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Humira 40 mg, single subcutaneous injection in abdomen or upper front of either thigh every 2 weeks for 22 weeks.

Number of subjects in period 2	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)
Started	213	214
Completed	201	194
Not completed	12	20
Consent withdrawn by subject	1	7
Physician decision	2	2
Unspecified	9	10
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Humira (Adalimumab)
Reporting group description:	
All subjects received Humira 40 milligrams (mg) once every 2 weeks subcutaneously for 10 weeks during Treatment Period 1 (TP1).	

Reporting group values	Humira (Adalimumab)	Total	
Number of subjects	445	445	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	369	369	
From 65-84 years	76	76	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	53.60		
standard deviation	± 11.17	-	
Sex: Female, Male Units: Subjects			
Female	368	368	
Male	77	77	
Ethnicity Units: Subjects			
Hispanic or Latino	4	4	
Not Hispanic or Latino	440	440	
Unknown or Not Reported	1	1	
Race Units: Subjects			
Black or African American	2	2	
White	440	440	
Unknown or Not Reported	3	3	

End points

End points reporting groups

Reporting group title	Humira (Adalimumab)
Reporting group description:	
All subjects received Humira 40 milligrams (mg) once every 2 weeks subcutaneously for 10 weeks during Treatment Period 1 (TP1).	
Reporting group title	Switching Arm: Humira and PF-06410293 (Adalimumab)
Reporting group description:	
Subjects after completing TP1, were randomised to receive PF-06410293 40 mg once every 2 weeks subcutaneously for 6 weeks during Treatment Period 2 (TP2). TP2 was followed by Treatment Period 3 (TP3). In TP3 subjects received Humira 40 mg once every 2 weeks subcutaneously for another 6 weeks. TP3 was followed by Treatment Period 4 (TP4). In TP4 subjects received PF-06410293 40 mg once every 2 weeks subcutaneously for next 10 weeks. Subjects were followed for 4 weeks post last dose.	
Reporting group title	Non-switching Arm: Humira (Adalimumab)
Reporting group description:	
Subjects after completing TP1, were randomised to continue treatment with Humira 40 mg once every 2 weeks subcutaneously for 22 weeks. Subjects were followed for 4 weeks post last dose.	

Primary: Maximum Observed Serum Concentration (Cmax) of Adalimumab

End point title	Maximum Observed Serum Concentration (Cmax) of Adalimumab
End point description:	
Cmax refers to maximum observed serum concentration of drug. Pharmacokinetic (PK) population included all randomised subjects who were dosed to initiate the Week 30 steady-state PK profile and remained on background methotrexate with no major protocol deviations influencing the PK assessment. The geometric coefficient of variation is expressed in percentage. Here, "Number of Subjects Analysed" signifies subjects evaluable for this endpoint. Since time points for analysis for this endpoint were falling in TP4, hence only switching and non-switching arms data were reported.	
End point type	Primary
End point timeframe:	
Pre-dose, 48, 72, 96, 144, 240 and 336 hours post dose on Day 211 (Week 30)	

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	186		
Units: Micrograms per millilitre				
geometric mean (geometric coefficient of variation)	9.156 (± 97)	8.974 (± 97)		

Statistical analyses

Statistical analysis title	Switching Arm vs. Non-switching Arm
Statistical analysis description:	
Equivalence was to be determined if the 90% confidence interval of the geometric mean ratio falls within	

the 80% to 125% range.

Comparison groups	Switching Arm: Humira and PF-06410293 (Adalimumab) v Non-switching Arm: Humira (Adalimumab)
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Geometric mean ratio (percentage)
Point estimate	102.56
Confidence interval	
level	90 %
sides	2-sided
lower limit	89.78
upper limit	117.17

Notes:

[1] - Analysis was performed using analysis of variance (ANOVA) model.

Primary: Area Under the Serum Concentration-Time Curve Over the Dosing Interval (AUCtau) of Adalimumab

End point title	Area Under the Serum Concentration-Time Curve Over the Dosing Interval (AUCtau) of Adalimumab

End point description:

Area under the serum concentration curve (AUC) from time 0 to end of dosing interval (tau), where dosing interval was once every two weeks. PK population included all randomised subjects who were dosed to initiate the Week 30 steady state PK profile and remained on background methotrexate with no major protocol deviations influencing the PK assessment. The geometric coefficient of variation is expressed in percentage. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point. Since time points for analysis for this end point were falling in TP4, hence only switching and non-switching arms data were reported.

End point type	Primary

End point timeframe:

Pre-dose, 48, 72, 96, 144, 240 and 336 hours post dose on Day 211 (Week 30)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	183		
Units: Microgram*hour per millilitre				
geometric mean (geometric coefficient of variation)	2472 (± 129)	2365 (± 133)		

Statistical analyses

Statistical analysis title	Switching Arm vs. Non-switching Arm

Statistical analysis description:

Equivalence was to be determined if the 90% confidence interval of the geometric mean ratio falls within the 80% to 125% range.

Comparison groups	Switching Arm: Humira and PF-06410293 (Adalimumab) v Non-switching Arm: Humira (Adalimumab)

Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	Geometric mean ratio (Percentage)
Point estimate	105.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	89.16
upper limit	124.39

Notes:

[2] - Analysis was performed using ANOVA model.

Secondary: Pre-dose Serum Concentration During Multiple Dosing (Ctrough) of Adalimumab

End point title	Pre-dose Serum Concentration During Multiple Dosing (Ctrough) of Adalimumab

End point description:

Ctrough was defined as pre-dose serum concentration during multiple dosing and observed directly from data. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10. Data for Days 1 and 71 were identified retrospectively for subjects in the safety randomised population, hence included in the switching and non-switching reporting groups. Here, n signifies subjects evaluable for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1, 71,113, 155, 169, 183, 197 and 211

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Micrograms per millilitre				
arithmetic mean (standard deviation)				
Day 1 (n=213, 214)	0.03102 (± 0.15291)	0.05703 (± 0.29719)		
Day 71 (n=211, 214)	6.999 (± 4.4196)	6.675 (± 4.3310)		
Day 113 (n=210, 209)	7.763 (± 5.0812)	7.374 (± 4.8807)		
Day 155 (n=208, 200)	7.900 (± 5.2493)	7.558 (± 5.0502)		
Day 169 (n=204, 197)	7.918 (± 5.1756)	7.767 (± 5.1860)		
Day 183 (n=202,197)	8.259 (± 5.3404)	7.933 (± 5.1299)		
Day 197 (n=204, 197)	8.347 (± 5.5458)	8.022 (± 5.2046)		
Day 211 (n=206, 198)	8.477 (± 5.4604)	7.891 (± 5.1818)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F) of Serum Adalimumab

End point title	Apparent Clearance (CL/F) of Serum Adalimumab

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolised or eliminated by normal biological processes. CL/F was calculated as dose administered divided by area under the concentration curve from time 0 extrapolated to infinite time (AUCinf). PK population included all randomised subjects who were dosed to initiate the Week 30 steady state PK profile and remained on background methotrexate with no major protocol deviations influencing the PK assessment. The geometric coefficient of variation is expressed in percentage. Here "Number of Subjects Analysed' signifies subjects evaluable for this end point. Since time points for analysis for this end point were falling in TP4, hence only switching and non-switching arms data were reported.

End point type	Secondary

End point timeframe:

Pre-dose, 48, 72, 96, 144, 240 and 336 hours post dose on Day 211 (Week 30)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	183		
Units: Millilitre per hour				
geometric mean (geometric coefficient of variation)	16.19 (± 129)	16.91 (± 133)		

Statistical analyses

No statistical analyses for this end point

Secondary: Average Serum Concentration (Cav) of Adalimumab

End point title	Average Serum Concentration (Cav) of Adalimumab

End point description:

Cav was defined as average serum concentration over the dosing interval. PK population included all randomised subjects who were dosed to initiate the Week 30 steady state PK profile and remained on background methotrexate with no major protocol deviations influencing the PK assessment. The geometric coefficient of variation is expressed in percentage. Here "Number of Subjects Analysed" signifies subjects evaluable for this end point. Since time points for analysis for this end point were falling in TP4, hence only switching and non-switching arms data were reported.

End point type	Secondary

End point timeframe:

Pre-dose, 48, 72, 96, 144, 240 and 336 hours post dose on Day 211 (Week 30)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	183		
Units: Micrograms per millilitre				
geometric mean (geometric coefficient of variation)	7.357 (± 130)	7.040 (± 133)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Cmax (Tmax) of Adalimumab

End point title	Time to Reach Cmax (Tmax) of Adalimumab

End point description:

Tmax is the time taken (in hours) to reach the maximum serum drug concentration. PK population included all randomised subjects who were dosed to initiate the Week 30 steady state PK profile and remained on background methotrexate with no major protocol deviations influencing the PK assessment. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point. Since time points for analysis for this end point were falling in TP4, hence only switching and non-switching arms data were reported.

End point type	Secondary

End point timeframe:

Pre-dose, 48, 72, 96, 144, 240 and 336 hours post dose on Day 211 (Week 30)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	186		
Units: Hours				
median (full range (min-max))	71.80 (0.000 to 336)	72.00 (0.000 to 337)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs),

Serious TEAEs and Treatment Related TEAEs: TP1

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs and Treatment Related TEAEs: TP1

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; congenital anomaly/birth defect and other important medical events. Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. TEAE for TP1 was defined as any AE that occurred after the beginning of study treatment in TP1 and before the first dose of study treatment administration after randomisation in TP2. AEs included both serious and all non-serious AEs. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	445			
Units: Subjects				
TEAEs	107			
Serious TEAEs	13			
Treatment related TEAEs	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or Higher TEAEs: TP2 and Beyond

End point title	Number of Subjects With Grade 3 or Higher TEAEs: TP2 and Beyond

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP2 and beyond was defined as any AE that occurred after the first dose of study treatment administration after randomisation in TP2 and up to 4 weeks after last dose. AEs were graded using the Common Terminology Criteria for Adverse Events where, grade 1=mild AE; grade 2=moderate AE; grade 3=severe AE; grade 4= life-threatening consequences; urgent intervention indicated; and grade 5= death related to AE. Number of subject with grade 3 or higher TEAEs were presented. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects	5	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Grade 3 or Higher TEAEs: TP1

End point title	Number of Subjects With Grade 3 or Higher TEAEs: TP1

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP1 was defined as any AE that occurred after the beginning of study treatment in TP1 and before the first dose of study treatment administration after randomisation in TP2. AEs were graded using the Common Terminology Criteria for Adverse Events where, grade 1=mild AE; grade 2=moderate AE; grade 3=severe AE; grade 4= life-threatening consequences; urgent intervention indicated; and grade 5= death related to AE. Number of subjects with grade 3 or higher TEAEs were presented. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	445			
Units: Subjects	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs, Serious TEAEs and Treatment Related TEAEs: TP2 and Beyond

End point title	Number of Subjects With TEAEs, Serious TEAEs and Treatment Related TEAEs: TP2 and Beyond

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An SAE was any untoward medical occurrence that, at any dose:resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation;was life-threatening;resulted in persistent or significant disability/incapacity; congenital anomaly/birth defect and other important medical events. Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. TEAE for TP2 and beyond was defined as any AE that occurred after administering the first dose of study

treatment after randomisation in TP2 and up to 4 weeks after last dose. AEs included both serious and all non-serious AEs. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects				
TEAEs	82	62		
Serious TEAEs	3	8		
Treatment related TEAEs	19	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Discontinued Treatment and Study due to TEAEs: TP2 and Beyond

End point title	Number of Subjects who Discontinued Treatment and Study due to TEAEs: TP2 and Beyond

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP2 and beyond was defined as any AE that occurred after the first dose of study treatment administration after randomisation in TP2 and up to 4 weeks after last dose. AEs included both serious and all non-serious AEs. Subjects who discontinued treatment due to TEAEs were those who had an AE record indicating that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study. Subjects who discontinued from study due to TEAE were those who had an AE record indicating that the AE caused the subject to be discontinued from the study. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects				

Discontinued from treatment due to TEAEs	0	3		
Discontinued from study due to TEAEs	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Discontinued Treatment and Study due to TEAEs: TP1

End point title	Number of Subjects who Discontinued Treatment and Study due to TEAEs: TP1

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP1 was defined as any AE that occurred after the beginning of study treatment in TP1 and before the first dose of study treatment administration after randomisation in TP2. Subject who discontinued treatment due to TEAEs were those who had an AE record indicating that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study. Subjects who discontinued from study due to TEAE were those who had an AE record indicating that the AE caused the subject to be discontinued from the study. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	445			
Units: Subjects				
Discontinued from treatment due to TEAEs	3			
Discontinued from study due to TEAE	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potential Immunogenic AEs to Study Treatment: TP2 and Beyond Among Anti-drug Antibody (ADA) Positive Subjects During TP1

End point title	Number of Subjects With Potential Immunogenic AEs to Study Treatment: TP2 and Beyond Among Anti-drug Antibody (ADA) Positive Subjects During TP1

End point description:

In this end point, subjects who were antidrug antibody (ADA) positive during TP1 were assessed in TP2 and beyond per visit for their ADA status at the time of start of their potential immunogenic AEs including ISRs, medically (Med) evaluated board standard MedDRA query (SMQ) of potential

hypersensitivity (anaphylactic reactions, hypersensitivity and angioedema), medically evaluated AEs meeting Sampson criteria, cytokine storm and delayed immune responses (DIR). ADA positive was defined as ADA titer >=1.88. Safety randomised population included all subjects who were randomised and received at least one dose of investigational product following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this endpoint. Here, n signifies subjects evaluable for specific rows.

End point type	Secondary

End point timeframe:

TP 2 and beyond: Week (Wk) 16, 22, 24, 26, 28, 30, 32

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	59		
Units: Subjects				
Wk 16: ISR;n=55,57	0	1		
Wk 16:Med. evaluated Sampson criteria met;n=55,57	0	0		
Wk 16: AEs belonging to SMQ Group;n=55,57	0	0		
Wk 22: ISR;n=55,55	0	1		
Wk 22:Med. evaluated Sampson criteria met;n=55,55	0	0		
Wk 22: AEs belonging to SMQ Group;n=55,55	0	0		
Wk 24: ISR;n=55,54	0	1		
Wk 24:Med. evaluated Sampson criteria met;n=55,54	0	0		
Wk 24: AEs belonging to SMQ Group;n=55,54	0	1		
Wk 26: ISR;n=54,53	1	1		
Wk 26:Med. evaluated Sampson criteria met;n=54,53	0	0		
Wk 26: AEs belonging to SMQ Group;n=54,53	0	0		
Wk 28: ISR;n=55,53	0	1		
Wk 28:Med. evaluated Sampson criteria met;n=55,53	0	0		
Wk 28: AEs belonging to SMQ Group;n=55,53	0	0		
Wk 30: ISR;n=55,54	0	1		
Wk 30:Med. evaluated Sampson criteria met;n=55,54	0	0		
Wk 30: AEs belonging to SMQ Group;n=55,54	1	0		
Wk 32: ISR;n=54,59	0	0		
Wk 32:Med. evaluated Sampson criteria met;n=54,59	0	0		
Wk 32: AEs belonging to SMQ Group;n=54,59	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs of Special Interest: TP2 and Beyond

End point title	Number of Subjects With TEAEs of Special Interest: TP2 and Beyond

End point description:

AEs of special interest (AESI) included: hypersensitivity events (anaphylactic reaction, hypersensitivity, angioedema, delayed immune responses and injection site reactions [ISRs]); blood and lymphatic system events (white blood cell disorders and anaemias nonhaemolytic and marrow depression); cardiovascular events (cardiac failure, hypertension and myocardial infarction); demyelinating conditions, gastric/hepatic events (gastrointestinal perforation, ulceration, haemorrhage or obstruction and hepatic disorders); infections and infestations (including TB and other opportunistic infections); malignancies (neoplasms benign, malignant and unspecified [including cysts and polyps]) and lupus like syndrome. Number of subjects with any AESI were presented. Safety randomised population: all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects	58	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potential Immunogenic AEs to Study Treatment: TP2 and Beyond Among ADA Negative Subjects During TP1

End point title	Number of Subjects With Potential Immunogenic AEs to Study Treatment: TP2 and Beyond Among ADA Negative Subjects During TP1

End point description:

In this end point, subjects who were ADA negative during TP1 were assessed in TP2 and beyond per visit for their ADA status at the time of start of their potential immunogenic AEs including ISRs, medically (Med) evaluated board SMQ of potential hypersensitivity (anaphylactic reactions, hypersensitivity and angioedema), medically evaluated AEs meeting Sampson criteria, cytokine storm and DIR. ADA negative was defined as ADA titer <1.88. Safety randomised population included all subjects who were randomised and received at least one dose of investigational product following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point. Here, n signifies subjects evaluable for specific rows.

End point type	Secondary

End point timeframe:

TP 2 and beyond: Wk 16, 22, 24, 26, 28, 30, 32

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	155		
Units: Subjects				
Wk 16:ISR;n=153,152	4	2		
Wk 16:Med evaluated Sampson criteria met;n=153,152	0	0		
Wk 16:AEs belonging to SMQ Group;n=153,152	0	0		
Wk 22:ISR;n=151,147	1	1		
Wk 22:Med evaluated Sampson criteria met;n=151,147	0	0		
Wk 22:AEs belonging to SMQ Group;n=151,147	0	0		
Wk 24:ISR;n=150,145	0	2		
Wk 24:Med evaluated Sampson criteria met;n=150,145	0	0		
Wk 24: AEs belonging to SMQ Group;n=150, 145	0	0		
Wk 26: ISR;n=148, 145	0	2		
Wk 26:Med evaluated Sampson criteria met;n=148,145	0	0		
Wk 26:AEs belonging to SMQ Group;n=148,145	0	0		
Wk 28:ISR;n=148,144	0	1		
Wk 28:Med evaluated Sampson criteria met;n=148,144	0	0		
Wk 28:AEs belonging to SMQ Group;n=148,144	0	0		
Wk 30:ISR;n=149,144	0	1		
Wk 30:Med evaluated Sampson criteria met;n=149,144	0	0		
Wk 30:AEs belonging to SMQ Group;n=149,144	0	0		
Wk 32:ISR;n=152,149	0	1		
Wk 32:Med evaluated Sampson criteria met;n=152,149	0	0		
Wk 32:AEs belonging to SMQ Group;n=152,149	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs and Serious TEAEs Related to COVID-19: TP1

End point title	Number of Subjects With TEAEs and Serious TEAEs Related to COVID-19: TP1

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; congenital anomaly/birth defect and other important medical events. TEAE for TP1 was defined as any AE that occurred after the beginning of study treatment in TP1 and before the first dose of study treatment administration after randomisation in TP2. AEs included both serious and all non-serious AEs. TEAEs and serious TEAEs related to Covid-19 as per investigator's assessment were presented. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	445			
Units: Subjects				
TEAE	10			
Serious TEAE	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Discontinued Treatment and Study due to TEAEs Related to COVID-19: TP1

End point title	Number of Subjects who Discontinued Treatment and Study due to TEAEs Related to COVID-19: TP1

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP1 was defined as any AE that occurred after the beginning of study treatment in TP1 and before the first dose of study treatment administration after randomisation in TP2. Subjects who discontinued treatment due to TEAEs were those who had an AE record indicating that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study. Subjects who discontinued from study due to TEAE were those who had an AE record indicating that the AE caused the subjects to be discontinued from the study. TEAEs were related to Covid-19. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	445			
Units: Subjects				
Discontinued from treatment due to TEAEs	0			
Discontinued from study due to TEAE	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Discontinued Treatment and Study due to TEAEs Related to COVID-19: TP2 and Beyond

End point title	Number of Subjects who Discontinued Treatment and Study due to TEAEs Related to COVID-19: TP2 and Beyond

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAE for TP2 and beyond was defined as any AE that occurred after the first dose of study treatment administration after randomisation in TP2 and up to 4 weeks after last dose. AEs included both serious and all non-serious AEs. Subjects who discontinued treatment due to TEAEs were those who had an AE record indicating that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study. Subjects who discontinued from study due to TEAE were those who had an AE record indicating that the AE caused the subject to be discontinued from the study. TEAEs were related to Covid-19. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects				
Discontinued from treatment due to TEAEs	0	0		
Discontinued from study due to TEAE	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs and Serious TEAEs Related to COVID-19: TP2 and Beyond

End point title	Number of Subjects With TEAEs and Serious TEAEs Related to COVID-19: TP2 and Beyond

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/incapacity; congenital anomaly/birth defect and other important medical events. TEAE for TP2 and beyond was defined as any AE that occurred after the first dose of study treatment administration after randomisation in TP2 and up to 4 weeks after last dose. AEs included both serious and all non-serious AEs. TEAEs and serious TEAEs related to Covid-19 as per investigator's assessment were presented. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10.

End point type	Secondary

End point timeframe:

Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects				
TEAE	20	16		
Serious TEAE	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects With Haematology Results by Maximum Common Toxicity Criteria (CTC) Grade: TP2 and Beyond

End point title	Number of subjects With Haematology Results by Maximum Common Toxicity Criteria (CTC) Grade: TP2 and Beyond

End point description:

Blood samples were collected for the analysis of following haematology parameters included: anaemia, haemoglobin increased, leucocytosis, lymphocyte count decreased, lymphocyte count increased, neutrophil count decreased, platelet count decreased, white blood cell decreased. Laboratory parameters were graded according to National Cancer Institute-CTC version 4.03 where, Grade 0: within normal limits; Grade1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life-threatening consequences and Grade 5: death. Categories with at least 1 non-zero value were reported in this end point. Safety randomised population included all subjects who were randomised and received at least one dose of dose of investigational product following the randomisation at Study Week 10. Here, “Number of Subjects Analysed” signifies subjects evaluable for this end point. Here, n signifies subjects evaluable for each row.

End point type	Secondary

End point timeframe:

Post randomisation up to end of study treatment (maximum of 22 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	205		
Units: Subjects				
Grade 0: Anaemia (n=209, 205)	198	190		
Grade 0: Haemoglobin increased (n=209, 205)	207	201		
Grade 0: Leucocytosis (n=209, 205)	209	205		
Grade 0: Lymphocyte count decreased (n=209, 205)	204	200		
Grade 0: Lymphocyte count increased (n=209, 205)	203	196		
Grade 0: Neutrophil count decreased (n=209, 204)	198	197		
Grade 0: Platelet count decreased (n=207, 204)	201	200		
Grade 0: White blood cell decreased (n=209, 205)	202	199		
Grade 1: Anaemia (n=209, 205)	5	7		
Grade 1: Haemoglobin increased (n=209, 205)	2	3		
Grade 1: Lymphocyte count decreased (n=209, 205)	4	3		
Grade 1: Neutrophil count decreased (n=209, 204)	4	3		
Grade 1: Platelet count decreased (n=207, 204)	6	4		
Grade 1: White blood cell decreased (n=209, 205)	6	6		
Grade 2: Anaemia (n=209, 205)	6	6		
Grade 2: Hemoglobin increased (n=209, 205)	0	1		
Grade 2: Lymphocyte count decreased (n=209, 205)	1	2		
Grade 2: Lymphocyte count increased (n=209, 205)	6	9		
Grade 2: Neutrophil count decreased (n=209, 204)	7	4		
Grade 2: White blood cell decreased (n=209, 205)	1	0		
Grade 3: Anaemia (n=209, 205)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities: TP1

End point title	Number of Subjects With Laboratory Abnormalities: TP1

End point description:

Blood samples were collected for the analysis of following laboratory parameters: haematology parameters (haemoglobin, erythrocyte mean corpuscular volume, erythrocyte mean corpuscular haemoglobin, erythrocyte mean corpuscular haemoglobin concentration platelet count, leukocytes, lymphocytes, neutrophils, eosinophils, monocytes); clinical chemistry parameters (bilirubin, alanine

aminotransferase [ALT], blood urea nitrogen [BUN], creatinine, potassium, bicarbonate); urine parameters: urine protein, urine haemoglobin, nitrite, leukocyte esterase and bacteria. Number of subjects with any laboratory abnormalities is presented. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1. Here "Number of subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 10 Weeks

End point values	Humira (Adalimumab)			
Subject group type	Reporting group			
Number of subjects analysed	437			
Units: Subjects	134			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities: TP2 and Beyond

End point title	Number of Subjects With Laboratory Abnormalities: TP2 and Beyond

End point description:

Blood samples were collected for the analysis of following laboratory parameters: haematology parameters (haemoglobin, erythrocyte mean corpuscular volume, erythrocyte mean corpuscular haemoglobin, erythrocyte mean corpuscular haemoglobin concentration platelet count, leukocytes, lymphocytes, neutrophils, eosinophils, monocytes); clinical chemistry parameters (bilirubin, ALT, BUN, creatinine, potassium, bicarbonate); urine parameters: urine protein, urine haemoglobin, nitrite, leukocyte esterase and bacteria. Number of subjects with any laboratory abnormalities is presented. Safety population for TP1 included all subjects who were enrolled and received at least one dose of study treatment in TP1. Safety randomised population included all subjects who were randomised and received at least one dose of dose of investigational product following the randomisation at Study Week 10. Here "Number of subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Post randomisation up to end of study treatment (maximum of 22 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	208		
Units: Subjects	71	83		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Chemistry Results by Maximum CTC Grade: TP2 and Beyond

End point title	Number of Subjects With Chemistry Results by Maximum CTC Grade: TP2 and Beyond

End point description:

Blood samples were collected for analysis of clinical chemistry parameters: (ALT increased, alkaline phosphatase (ALP) increased , aspartate aminotransferase (AST) increased , blood bilirubin increased, creatinine increased, hypercalcemia, hyperkalemia, hypernatremia, hypoalbuminemia, hypocalcemia, hypokalemia, hyponatremia. Laboratory parameters were graded according to NCI-CTC version 4.03 where, grade 0= within normal limits; Grade1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life-threatening consequences and Grade 5: death. Categories with at least 1 non-zero value were reported in this end point. Safety randomised population included all subjects who were randomised and received at least one dose of dose of investigational product following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point. Here, n signifies subjects evaluable for each row.

End point type	Secondary

End point timeframe:

Post randomisation up to end of study treatment (maximum of 22 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	208		
Units: Subjects				
Grade 0: ALT increased (n=211, 208)	169	174		
Grade 0: ALP increased (n=211, 208)	202	196		
Grade 0: AST increased (n=211, 208)	195	198		
Grade 0: Blood bilirubin increased (n=211, 208)	205	204		
Grade 0: Creatinine increased (n=211, 208)	171	151		
Grade 0: Hypercalcemia (n=211, 208)	211	207		
Grade 0: Hyperkalaemia (n=212, 208)	208	202		
Grade 0: Hypernatremia (n=212, 208)	210	207		
Grade 0: Hypoalbuminemia (n=212, 208)	212	208		
Grade 0: Hypocalcemia (n=211, 208)	201	202		
Grade 0: Hypokalemia (n=212, 208)	210	207		
Grade 0: Hyponatremia (n=212, 208)	211	207		
Grade 1: ALT increased (n=211, 208)	40	33		
Grade 1: ALP increased (n=211, 208)	9	12		
Grade 1: AST increased (n=211, 208)	16	10		
Grade 1: Blood bilirubin increased (n=211, 208)	5	3		
Grade 1: Creatinine increased (n=211, 208)	39	52		
Grade 1: Hypercalcemia (n=211, 208)	0	1		
Grade 1: Hyperkalemia (n=212, 208)	4	6		

Grade 1: Hypernatremia (n=212, 208)	2	1		
Grade 1: Hypocalcemia (n=211, 208)	10	6		
Grade 1: Hyponatremia (n=212, 208)	1	1		
Grade 2: ALT increased (n=211, 208)	2	1		
Grade 2: Blood bilirubin increased (n=211, 208)	1	1		
Grade 2: Creatinine increased (n=211, 208)	1	5		
Grade 2: Hypokalaemia (n=212, 208)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Laboratory Results Based on Evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) Analysis: TP2 and Beyond

End point title	Number of Subjects with Laboratory Results Based on Evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) Analysis: TP2 and Beyond

End point description:

In this end point, liver function laboratory parameters, which included: normal bilirubin (bil.) and AST/ALT, Temple's Corollary (AST/ALT more than or equal to [>=]3*upper limit normal [ULN] and normal bilirubin), Gilbert's Syndrome (GS) or cholestasis (normal AST/ALT and bilirubin >=2*ULN) and Potential (Pot.) Hy's Law Cases (AST/ALT >=3*ULN and Bilirubin>=2*ULN) according to eDISH criteria, were reported. Safety randomised population included all subjects who were randomised and received at least one dose of dose of investigational product following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Post randomisation up to end of study treatment (maximum of 22 weeks)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	208		
Units: Subjects				
Normal Bilirubin and AST/ALT	208	207		
Temple's Corollary(AST/ALT>=3*ULN and Normal Bil.)	2	1		
GS or Cholestasis (Normal AST/ALT and Bil >=2*ULN)	1	0		
Pot Hy's Law Cases(AST/ALT>=3*ULN and Bil.>=2*ULN)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline, Absolute Week 32 Values for Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Change From Baseline in SBP, DBP at Week 32 ([EOT]/[ET])

End point title	Baseline, Absolute Week 32 Values for Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Change From Baseline in SBP, DBP at Week 32 ([EOT]/[ET])

End point description:

SBP and DBP were measured in a supine position using an automated device preceded by at least 5 minutes of rest for the subject in a quiet setting without any distractions. Baseline value was defined as the most recent measurement prior to the first dose of study treatment after randomisation in TP2. Safety randomised population included all subjects who were randomised and received at least one dose of dose of investigational product following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline and Week 32 (end of treatment [EOT]/early termination [ET])

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	209		
Units: Millimetre of mercury				
arithmetic mean (standard deviation)				
SBP: Baseline	125.7 (± 12.72)	125.9 (± 11.49)		
SBP: Absolute value at Week 32 (EOT/ET)	126.0 (± 11.20)	126.2 (± 12.69)		
SBP: Change at Week 32 (EOT/ET)	0.3 (± 11.49)	0.4 (± 11.28)		
DBP: Baseline	78.1 (± 8.31)	77.7 (± 7.60)		
DBP: Absolute value at Week 32 (EOT/ET)	78.6 (± 7.77)	77.5 (± 7.54)		
DBP: Change at Week 32 (EOT/ET)	0.5 (± 8.04)	-0.2 (± 8.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline, Absolute Week 32 Values for Temperature and Change From Baseline in Temperature at Week 32 (EOT/ET)

End point title	Baseline, Absolute Week 32 Values for Temperature and Change From Baseline in Temperature at Week 32 (EOT/ET)

End point description:

Baseline value was defined as the most recent measurement prior to the first dose of study treatment after randomisation in TP2. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline and Week 32 (EOT/ET)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	209		
Units: Degree Celsius				
arithmetic mean (standard deviation)				
Baseline	36.5 (± 0.27)	36.5 (± 0.27)		
Absolute at Week 32 (EOT/ET)	36.4 (± 0.26)	36.4 (± 0.20)		
Change at Week 32 (EOT/ET)	-0.0 (± 0.28)	-0.0 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline, Absolute Week 32 Values for Pulse Rate and Change From Baseline in Pulse Rate at Week 32 (EOT/ET)

End point title	Baseline, Absolute Week 32 Values for Pulse Rate and Change From Baseline in Pulse Rate at Week 32 (EOT/ET)

End point description:

Pulse rate was measured in a supine position using an automated device preceded by at least 5 minutes of rest for the subject in a quiet setting without any distractions. Baseline value was defined as the most recent measurement prior to the first dose of study treatment after randomisation in TP2. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline and Week 32 (EOT/ET)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	209		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Baseline	73.6 (± 8.55)	73.2 (± 8.42)		
Absolute value at Week 32 (EOT/ET)	73.6 (± 7.94)	73.1 (± 7.98)		
Change at Week 32 (EOT/ET)	0.1 (± 8.55)	-0.2 (± 7.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline, Absolute Week 32 Values for Respiratory Rate and Change From Baseline in Respiratory Rate at Week 32 (EOT/ET)

End point title	Baseline, Absolute Week 32 Values for Respiratory Rate and Change From Baseline in Respiratory Rate at Week 32 (EOT/ET)

End point description:

Baseline value was defined as the most recent measurement prior to the first dose of study treatment after randomisation in TP2. Safety randomised population included all subjects who were randomised and received at least one dose of study treatment following the randomisation at Study Week 10. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline and Week 32 (EOT/ET)

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	209		
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Baseline	16.6 (± 1.75)	16.6 (± 2.10)		
Absolute at Week 32 (EOT/ET)	16.5 (± 1.81)	16.6 (± 2.00)		
Change at Week 32 (EOT/ET)	-0.1 (± 1.36)	-0.0 (± 1.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Were Anti-Drug Antibodies (ADA) Positive and Neutralizing Antibodies (NAb) Positive

End point title	Number of Subjects who Were Anti-Drug Antibodies (ADA) Positive and Neutralizing Antibodies (NAb) Positive

End point description:

Serum samples were analysed using a validated electrochemoluminescent (ECL) immunoassay for ADA assessment. Samples positive for ADA were further tested for neutralising activity using a validated cell based NAb assay. ADA positive was defined as ADA titer >=1.88 while NAb positive was defined as NAb titer >=0.70. Safety randomised population included all subjects who were randomised and received at least one dose of investigational product following the randomisation at Study Week 10. For ADA: n= all

subjects assessed for ADA measurement at specific time points. For Nab: n= all subjects with ADA positive results assessed for Nab measurement at specific time points.

End point type	Secondary

End point timeframe:

Week 10, 16, 22, 24, 26, 28, 30, 32

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Subjects				
Week 10: ADA positive (n=213, 214)	55	59		
Week 10: NAb positive (n=55, 59)	22	19		
Week 16: ADA positive (n=213, 214)	88	97		
Week 16: NAb positive (n=88, 97)	22	21		
Week 22: ADA positive (n=213, 214)	96	106		
Week 22: NAb positive (n=96, 106)	24	20		
Week 24: ADA positive (n=213, 214)	102	100		
Week 24: NAb positive (n=102, 100)	19	20		
Week 26: ADA positive (n=213, 214)	101	105		
Week 26: NAb positive (n=101, 105)	21	15		
Week 28: ADA positive (n=213, 214)	102	105		
Week 28: NAb positive (n=102, 105)	18	16		
Week 30: ADA positive (n=213, 214)	103	109		
Week 30: NAb positive (n=103, 109)	17	19		
Week 32: ADA positive (n=213, 214)	100	104		
Week 32: NAb positive (n=100, 104)	18	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean ADA Titers

End point title	Mean ADA Titers

End point description:

Serum samples were analysed using a validated ECL immunoassay for ADA assessment. Endpoint titer was defined as log10 of the reciprocal of the ADA serum dilution at which the sample response was equal to the cut-point of the assay. Safety randomised population included all subjects who were randomised and received at least one dose of investigational product following the randomisation at Study Week 10. Here, n signifies subjects evaluable with ADA non-missing values at specific time points.

End point type	Secondary

End point timeframe:

Week 10, 16, 22, 24, 26, 28, 30, 32

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Endpoint titer				
arithmetic mean (standard deviation)				
Week 10 (n=211, 214)	0.830 (± 1.46534)	0.880 (± 1.51789)		
Week 16 (n=210, 209)	1.385 (± 1.71192)	1.546 (± 1.75299)		
Week 22 (n=208, 202)	1.570 (± 1.77364)	1.784 (± 1.79136)		
Week 24 (n=207, 199)	1.674 (± 1.78148)	1.709 (± 1.78301)		
Week 26 (n=204, 198)	1.671 (± 1.77780)	1.806 (± 1.78134)		
Week 28 (n=205, 197)	1.670 (± 1.77759)	1.788 (± 1.77325)		
Week 30 (n=206, 198)	1.658 (± 1.75135)	1.854 (± 1.78187)		
Week 32 (n=199, 193)	1.677 (± 1.76060)	1.846 (± 1.81474)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean NAb Titers

End point title	Mean NAb Titers

End point description:

Serum samples were analysed using a validated ECL immunoassay for ADA assessment. Endpoint titer was defined as log10 of the reciprocal of the NAb serum dilution at which the sample response was equal to the cut-point of the assay. Safety randomised population included all subjects who were randomised and received at least one dose of investigational product following the randomisation at Study Week 10. Here, n signifies subjects evaluable with NAb non-missing values at specific time points.

End point type	Secondary

End point timeframe:

Week 10, 16, 22, 24, 26, 28, 30, 32

End point values	Switching Arm: Humira and PF-06410293 (Adalimumab)	Non-switching Arm: Humira (Adalimumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	214		
Units: Endpoint titer				
arithmetic mean (standard deviation)				
Week 10 (n=55, 58)	0.712 (± 1.02024)	0.718 (± 1.14660)		
Week 16 (n=88, 97)	0.467 (± 0.90051)	0.443 (± 0.92450)		
Week 22 (n=96, 106)	0.488 (± 0.91641)	0.405 (± 0.89940)		
Week 24 (n=102, 100)	0.396 (± 0.87759)	0.409 (± 0.90030)		
Week 26 (n=101, 105)	0.420 (± 0.90500)	0.328 (± 0.84792)		
Week 28 (n=102, 105)	0.360 (± 0.83177)	0.353 (± 0.88464)		
Week 30 (n=103, 109)	0.359 (± 0.87754)	0.377 (± 0.91439)		
Week 32 (n=100, 104)	0.341 (± 0.81482)	0.362 (± 0.88055)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TP1: Day 1 up to maximum of 10 Weeks
TP2 and beyond: Post randomisation up to maximum of 4 weeks after last dose (maximum of 26 weeks)

Adverse event reporting additional description:

Same event may appear as both AE and SAE but are distinct events. Event may be categorised serious in 1 subject and non-serious in another,or 1 subject may have experienced both serious and non-serious event during study. For TP1 (Humira arm), Safety-TP1 population. For TP2 and beyond (switching and non-switching arm), Safety-randomised population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Humira (Adalimumab)

Reporting group description:

All subjects received Humira 40 mg once every 2 weeks subcutaneously for 10 weeks during TP1.

Reporting group title	Non-switching Arm: Humira (Adalimumab)

Reporting group description:

Subjects after completing TP1, were randomised to continue treatment with Humira 40 mg once every 2 weeks subcutaneously for 22 weeks. Subjects were followed for 4 weeks post last dose.

Reporting group title	Switching Arm: Humira and PF-06410293 (Adalimumab)

Reporting group description:

Subjects after completing TP1, were randomised to receive PF-06410293 40 mg once every 2 weeks subcutaneously for 6 weeks during TP2. TP2 was followed by TP3. In TP3 subjects received Humira 40 mg once every 2 weeks subcutaneously for another 6 weeks. TP3 was followed by TP4. In TP4 subjects received PF-06410293 40 mg once every 2 weeks subcutaneously for next 10 weeks. Subjects were followed for 4 weeks post last dose.

Serious adverse events	Humira (Adalimumab)	Non-switching Arm: Humira (Adalimumab)	Switching Arm: Humira and PF-06410293 (Adalimumab)
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 445 (2.92%)	8 / 214 (3.74%)	3 / 213 (1.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian cancer metastatic			
subjects affected / exposed	1 / 445 (0.22%)	0 / 214 (0.00%)	0 / 213 (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
Injury, poisoning and procedural complications			

Subdural haemorrhage			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	0 / 213 (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
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	0 / 213 (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
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	0 / 213 (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
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 445 (0.00%)	0 / 214 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	1 / 445 (0.22%)	0 / 214 (0.00%)	0 / 213 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 445 (0.22%)	0 / 214 (0.00%)	0 / 213 (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
Cholecystitis acute			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	0 / 213 (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
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 445 (0.22%)	0 / 214 (0.00%)	0 / 213 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	5 / 445 (1.12%)	1 / 214 (0.47%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 445 (0.22%)	2 / 214 (0.93%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 445 (0.00%)	0 / 214 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 445 (0.22%)	1 / 214 (0.47%)	0 / 213 (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
Lyme disease			
subjects affected / exposed	2 / 445 (0.45%)	0 / 214 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 445 (0.22%)	0 / 214 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Humira (Adalimumab)	Non-switching Arm: Humira (Adalimumab)	Switching Arm: Humira and PF-06410293 (Adalimumab)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 445 (6.29%)	38 / 214 (17.76%)	46 / 213 (21.60%)
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	9 / 445 (2.02%)	14 / 214 (6.54%)	18 / 213 (8.45%)
occurrences (all)	9	14	19
Alanine aminotransferase increased			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	3 / 213 (1.41%)
occurrences (all)	0	1	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	3 / 213 (1.41%)
occurrences (all)	0	1	3
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 445 (0.00%)	5 / 214 (2.34%)	2 / 213 (0.94%)
occurrences (all)	0	5	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 445 (0.00%)	4 / 214 (1.87%)	4 / 213 (1.88%)
occurrences (all)	0	4	4
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	13 / 445 (2.92%)	4 / 214 (1.87%)	6 / 213 (2.82%)
occurrences (all)	17	24	9
Swelling			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	3 / 213 (1.41%)
occurrences (all)	0	4	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 445 (0.00%)	0 / 214 (0.00%)	3 / 213 (1.41%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	3 / 213 (1.41%)
occurrences (all)	0	1	3
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	10 / 445 (2.25%)	4 / 214 (1.87%)	6 / 213 (2.82%)
occurrences (all)	17	24	9
Pruritus			
subjects affected / exposed	7 / 445 (1.57%)	0 / 214 (0.00%)	0 / 213 (0.00%)
occurrences (all)	9	0	0
Rash			
subjects affected / exposed	0 / 445 (0.00%)	0 / 214 (0.00%)	3 / 213 (1.41%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 445 (0.00%)	1 / 214 (0.47%)	3 / 213 (1.41%)
occurrences (all)	0	1	3
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 445 (1.12%)	3 / 214 (1.40%)	4 / 213 (1.88%)
occurrences (all)	5	3	5
COVID-19			
subjects affected / exposed	0 / 445 (0.00%)	9 / 214 (4.21%)	16 / 213 (7.51%)
occurrences (all)	0	9	18
Nasopharyngitis			
subjects affected / exposed	0 / 445 (0.00%)	7 / 214 (3.27%)	0 / 213 (0.00%)
occurrences (all)	0	7	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 445 (0.00%)	3 / 214 (1.40%)	3 / 213 (1.41%)
occurrences (all)	0	3	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2020	Added new Exclusion Criterion that unstable dose of oral and intramuscular (IM) corticosteroid is prohibited. Add clarification to Exclusion Criterion (3) that active significant infection e.g., SARS-CoV2 (COVID-19) infection and any active infection considered to be clinically significant by the investigator should be excluded.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2020	Enrollment, randomization, and screening for the study were paused at all sites.	06 May 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In subject disposition discontinuation due to AEs,were captured under different reasons (e.g. other, physician decision etc.) as study case report form (CRF) did not include AE as option for sites to record if discontinuation was due to AE.

Notes: