Clinical trial results:
A PHASE 3, MULTI-SITE, OPEN-LABEL STUDY OF THE LONG TERM SAFETY AND TOLERABILITY OF 2 ORAL DOSES OF CP-690,550 IN SUBJECTS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

Summary

EudraCT number	2010-020002-15
Trial protocol	CZ DE GB NL FI ES DK SE BG SK HU AT GR BE
Global end of trial date	22 June 2016

Results information

Result version number	v1 (current)
This version publication date	16 June 2017
First version publication date	16 June 2017

Trial information

Trial identification

Sponsor protocol code	A3921061

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01163253
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long term safety and tolerability of treatment with tofacitinib (10 mg twice a day [BID] or variable dose 5 and 10 mg BID) in adult subjects with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2010
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	Argentina: 19
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bosnia and Herzegovina: 12
Country: Number of subjects enrolled	Brazil: 7
Country: Number of subjects enrolled	Bulgaria: 56
Country: Number of subjects enrolled	Canada: 374
Country: Number of subjects enrolled	Chile: 171
Country: Number of subjects enrolled	Colombia: 74
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Czech Republic: 41
Country: Number of subjects enrolled	Denmark: 30
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 74
Country: Number of subjects enrolled	Germany: 229
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Hungary: 91

Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Poland: 293
Country: Number of subjects enrolled	Puerto Rico: 17
Country: Number of subjects enrolled	Russian Federation: 125
Country: Number of subjects enrolled	Serbia: 16
Country: Number of subjects enrolled	Singapore: 13
Country: Number of subjects enrolled	Slovakia: 20
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Sweden: 17
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Taiwan: 67
Country: Number of subjects enrolled	Ukraine: 234
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 679
Worldwide total number of subjects	2867
EEA total number of subjects	919

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)	2672
From 65 to 84 years	195
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 2881 subjects were enrolled in this study, however 2867 subjects received treatment.

Pre-assignment

Screening details:

The study was conducted at 282 sites in 36 countries. The start date of the study was 17-Sep-2010 and the study completed on 22-Jun-2016.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Open-Label

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib 10 mg

Arm description:

Subjects received Tofacitinib 10 milligram (mg) tablets orally twice daily from Day 1 until any safety finding requiring study discontinuation (up to a maximum of 66 months).

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

Dosage and administration details:

Subjects received Tofacitinib 10 mg twice daily from Day 1 until any safety finding requiring study discontinuation (up to a maximum of 66 months).

Arm title	Tofacitinib 5 mg or 10 mg

Arm description:

Subjects received Tofacitinib 10 mg tablets orally twice daily for a period of 3 months. After 3 months of treatment, subjects received twice daily dosing of tofacitinib 5 mg or 10 mg tablets until any safety and efficacy finding requiring study discontinuation (up to a maximum of 66 months). Dose adjustment (5 mg or 10 mg) was assessed on every 3 month visit and was based on investigator’s discretion.

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

Dosage and administration details:

Subjects received Tofacitinib 10 mg twice daily for a period of 3 months. After 3 months of treatment, subjects received twice daily dosing of tofacitinib 5 mg or 10 mg until any safety and efficacy finding requiring study discontinuation (up to a maximum of 66 months). Dose adjustment (5 mg or 10 mg) was assessed on every 3 month visit and was based on investigator’s discretion.

Number of subjects in period 1	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg
Started	2281	586
Completed	0	0
Not completed	2281	586
Withdrawn Due to Pregnancy	12	2
Adverse Event	300	78
Lost to Follow-up	125	23
Death	17	5
Ongoing	13	4
Insufficient Clinical Response	423	29
Withdrawal by Subject	199	50
Study Terminated by Sponsor	978	349
Medication Error	1	-
Protocol deviation	43	12
Other Unspecified	170	34

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib 10 mg
Reporting group description:	
Subjects received Tofacitinib 10 milligram (mg) tablets orally twice daily from Day 1 until any safety finding requiring study discontinuation (up to a maximum of 66 months).	
Reporting group title	Tofacitinib 5 mg or 10 mg
Reporting group description:	
Subjects received Tofacitinib 10 mg tablets orally twice daily for a period of 3 months. After 3 months of treatment, subjects received twice daily dosing of tofacitinib 5 mg or 10 mg tablets until any safety and efficacy finding requiring study discontinuation (up to a maximum of 66 months). Dose adjustment (5 mg or 10 mg) was assessed on every 3 month visit and was based on investigator's discretion.	

Reporting group values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg	Total
Number of subjects	2281	586	2867
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2137	535	2672
From 65-84 years	144	51	195
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	45.3	47	
standard deviation	± 12.5	± 13	-
Gender Categorical Units: Subjects			
Female	640	203	843
Male	1641	383	2024

End points

End points reporting groups

Reporting group title	Tofacitinib 10 mg

Reporting group description:

Subjects received Tofacitinib 10 milligram (mg) tablets orally twice daily from Day 1 until any safety finding requiring study discontinuation (up to a maximum of 66 months).

Reporting group title	Tofacitinib 5 mg or 10 mg

Reporting group description:

Subjects received Tofacitinib 10 mg tablets orally twice daily for a period of 3 months. After 3 months of treatment, subjects received twice daily dosing of tofacitinib 5 mg or 10 mg tablets until any safety and efficacy finding requiring study discontinuation (up to a maximum of 66 months). Dose adjustment (5 mg or 10 mg) was assessed on every 3 month visit and was based on investigator's discretion.

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

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and up to 4 weeks after last dose (up to 67 months) that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious adverse events. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: subjects				
AEs	1876	490		
SAEs	304	88		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Adverse Events by Severity

End point title	Number of Adverse Events by Severity[2]

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. AEs were classified according to the severity in 3 categories: a) mild: AEs did not interfere with participant's usual function; b) moderate: AEs interfered to some extent with participant's usual function; c) severe: AEs interfered significantly with participant's usual function. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: adverse events				
Mild	5354	1749		
Moderate	3268	766		
Severe	410	136		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities[3]

End point description:

Abnormality criteria:hematology (hemoglobin,hematocrit,red blood cell <0.8*lower limit of normal [LLN];reticulocyte<0.5*LLN,>1.5*ULN; platelets<0.5*LLN,>1.75*upper limit of normal[ULN];WBC<0.6*LLN,>1.5*ULN;lymphocytes,neutrophils, basophils, eosinophils,monocytes<0.8*LLN; >1.2*ULN;coagulation(prothrombin [PT], PT ratio>1.1*ULN) liver function(bilirubin>1.5*ULN, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma GT>0.3*ULN, protein,albumin<0.8*LLN; >1.2*ULN, globulin<0.5*LLN; >1.5*ULN);renal function (blood urea nitrogen, creatinine>1.3*ULN);electrolytes(sodium<0.95* LLN; >1.05* ULN, potassium, chloride, calcium, bicarbonate<0.9*LLN; >1.1*ULN),chemistry (glucose<0.6*LLN; >1.5* ULN),urinalysis (pH <4.5;>8, glucose, ketones, protein, blood,urobilinogen, nitrite, bilirubin, leukocyte esterase>=1; RBC, WBC>=20); lipids (cholesterol [C], LDL-C >1.3*ULN, HDL-C<0.8*LLN, triglycerides>1.3* ULN), hormones(T4, T3, T4, TSH<0.8* LLN; >1.2* ULN).Safety

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2271	578		
Units: subjects	2203	565		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 1

End point title	Change From Baseline in Hemoglobin Level at Month 1[4]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug and 'n' signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2277	586		
Units: gram per deciliter (g/dL)				
arithmetic mean (standard deviation)				
Baseline (n =2277, 586)	14.64 (± 1.27)	14.64 (± 1.24)		
Change at Month 1 (n =2201, 563)	-0.24 (± 0.83)	-0.32 (± 0.86)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 3

End point title	Change From Baseline in Hemoglobin Level at Month 3[5]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2198	572		
Units: g/dL				
arithmetic mean (standard deviation)	-0.27 (± 0.85)	-0.39 (± 0.83)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 6

End point title	Change From Baseline in Hemoglobin Level at Month 6[6]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2051	563		
Units: g/dL				
arithmetic mean (standard deviation)	-0.27 (± 0.88)	-0.3 (± 0.87)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 12

End point title	Change From Baseline in Hemoglobin Level at Month 12[7]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1759	531		
Units: g/dL				
arithmetic mean (standard deviation)	-0.34 (± 0.93)	-0.3 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 24

End point title	Change From Baseline in Hemoglobin Level at Month 24[8]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1385	449		
Units: g/dL				
arithmetic mean (standard deviation)	-0.3 (± 0.96)	-0.29 (± 0.89)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 36

End point title	Change From Baseline in Hemoglobin Level at Month 36[9]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1114	380		
Units: g/dL				
arithmetic mean (standard deviation)	-0.32 (± 0.93)	-0.37 (± 0.88)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hemoglobin Level at Month 48

End point title	Change From Baseline in Hemoglobin Level at Month 48[10]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	415	127		
Units: g/dL				
arithmetic mean (standard deviation)	-0.35 (± 0.97)	-0.43 (± 0.94)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 1

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 1[11]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug and 'n' signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2275	586		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Baseline: Lymphocyte Count (n =2275, 586)	1.76 (± 0.57)	1.8 (± 0.56)		
Baseline: Neutrophil Count (n =2275, 586)	4.74 (± 1.68)	4.55 (± 1.7)		
Change at Month 1: Lymphocyte Count (n =2182, 559)	0.07 (± 0.52)	0.11 (± 0.56)		
Change at Month 1: Neutrophil Count (n =2182, 559)	-0.37 (± 1.65)	-0.48 (± 1.58)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 3

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 3[12]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2183	570		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte count	0 (± 0.52)	0.02 (± 0.52)		
Neutrophil Count	-0.28 (± 1.63)	-0.28 (± 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 6

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 6[13]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2034	559		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte Count	-0.11 (± 0.51)	-0.05 (± 0.51)		
Neutrophil Count	-0.25 (± 1.61)	-0.22 (± 1.64)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 12

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 12[14]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1751	530		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte Count	-0.21 (± 0.52)	-0.16 (± 0.48)		
Neutrophil Count	-0.23 (± 1.61)	-0.18 (± 1.58)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 24

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 24[15]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1377	445		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte Count	-0.28 (± 0.52)	-0.18 (± 0.54)		
Neutrophil Count	-0.19 (± 1.69)	-0.02 (± 1.59)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 36

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 36[16]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1111	377		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte Count	-0.35 (± 0.55)	-0.24 (± 0.51)		
Neutrophil Count	-0.26 (± 1.61)	-0.11 (± 1.68)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Lymphocyte and Neutrophil Count at Month 48

End point title	Change From Baseline in Lymphocyte and Neutrophil Count at Month 48[17]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	413	127		
Units: 1000 cells/mm^3				
arithmetic mean (standard deviation)				
Lymphocyte Count	-0.42 (± 0.52)	-0.27 (± 0.46)		
Neutrophil Count	-0.28 (± 1.7)	-0.07 (± 1.49)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 1

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 1[18]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and 'n' signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2278	586		
Units: milligram per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Baseline: Creatinine (n =2278, 586)	0.9 (± 0.17)	0.88 (± 0.16)		
Baseline: LDL-C (n =2253, 585)	114.14 (± 32.53)	115 (± 35.03)		
Baseline: HDL-C (n =2277, 586)	49.05 (± 13.93)	51.87 (± 17.33)		
Baseline: TC (n =2277, 586)	192.11 (± 38.1)	194.96 (± 39.79)		
Change at Month 1: Creatinine (n =2204, 563)	0.03 (± 0.1)	0.02 (± 0.1)		
Change at Month 1: LDL-C (n =2125, 546)	11.49 (± 28.77)	11.55 (± 29.55)		
Change at Month 1: HDL-C (n =2203, 562)	8.19 (± 9.89)	8.63 (± 10.5)		
Change at Month 1: TC (n =2203, 562)	21.12 (± 34.08)	22.65 (± 34.36)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 3

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 3[19]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2211	573		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =2211, 573)	0.04 (± 0.21)	0.03 (± 0.1)		
LDL-C (n =2130, 559)	11.97 (± 29.77)	10.44 (± 32.72)		
HDL-C (n =2204, 573)	7.69 (± 10.23)	7.96 (± 10.33)		
TC (n =2203, 573)	21.52 (± 35.63)	21.06 (± 38.34)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 6

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 6[20]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2057	564		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =2057, 564)	0.03 (± 0.11)	0.03 (± 0.1)		
LDL-C (n =1983, 553)	11.44 (± 30.1)	8.74 (± 33.22)		
HDL-C (n =2056, 564)	7.68 (± 10.33)	8.19 (± 11.6)		
TC (n =2057, 564)	20.91 (± 35.94)	19.17 (± 39.06)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 12

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 12[21]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1777	533		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =1777, 533)	0.04 (± 0.12)	0.04 (± 0.12)		
LDL-C (n =1728, 521)	11.31 (± 31.45)	9.65 (± 32.87)		
HDL-C (n =1776, 531)	8.13 (± 10.48)	6.88 (± 11.15)		
TC (n =1776, 531)	21.2 (± 39.15)	16.97 (± 37.84)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 24

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 24[22]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1398	450		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =1398, 450)	0.05 (± 0.11)	0.04 (± 0.11)		
LDL-C (n =1353, 435)	11.35 (± 35.33)	10.13 (± 35.67)		
HDL-C (n =1397, 450)	9.02 (± 11.62)	7.55 (± 11.94)		
TC (n =1398, 450)	21.74 (± 41.05)	19.22 (± 39.69)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 36

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 36[23]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1122	384		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =1122, 384)	0.05 (± 0.12)	0.04 (± 0.15)		
LDL-C (n =1085, 375)	10.11 (± 35.83)	7.25 (± 37.41)		
HDL-C (n =1119, 384)	8.8 (± 11.59)	6.39 (± 11.91)		
TC (n =1119, 384)	20.2 (± 41.28)	15.55 (± 43.59)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 48

End point title	Change From Baseline in Creatinine, Low-Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C) and Total Cholesterol (TC) Levels at Month 48[24]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	417	127		
Units: mg/dL				
arithmetic mean (standard deviation)				
Creatinine (n =417, 127)	0.04 (± 0.12)	0.04 (± 0.11)		
LDL-C (n =402, 123)	12.98 (± 36.89)	6.61 (± 34.66)		
HDL-C (n =417, 127)	8.62 (± 11.36)	8.19 (± 12.72)		
TC (n =417, 127)	24.99 (± 43.35)	16.36 (± 40.99)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 1

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 1[25]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2278	586		
Units: international unit per liter (IU/L)				
arithmetic mean (standard deviation)				
Baseline: AST (n =2278, 586)	24.02 (± 12.22)	24.66 (± 10.36)		
Baseline: ALT (n =2278, 586)	28.47 (± 17.29)	28.17 (± 16.56)		
Change at Month 1: AST (n =2198, 564)	3.48 (± 15.39)	4.07 (± 12.01)		
Change at Month 1: ALT (n =2199, 564)	4.07 (± 19.04)	4.84 (± 17.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 3

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 3[26]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2201	573		
Units: IU/L				
arithmetic mean (standard deviation)				
AST (n =2200, 573)	4.09 (± 17.75)	5.65 (± 16.37)		
ALT (n =2201, 573)	4.86 (± 18.52)	6.86 (± 20.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 6

End point title	Change From Baseline in Aspartate Aminotransferase (AST)

	and Alanine Aminotransferase (ALT) Levels at Month 6[27]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2054	564		
Units: IU/L				
arithmetic mean (standard deviation)				
AST (n =2052, 564)	4.5 (± 15.6)	5.07 (± 14.9)		
ALT (n =2054, 564)	5.98 (± 19)	6.15 (± 18.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 12

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 12[28]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1774	532		
Units: IU/L				
arithmetic mean (standard deviation)				
AST (n =1772, 531)	4.88 (± 16.63)	7.29 (± 22.7)		
ALT (n =1774, 532)	6.68 (± 23.12)	8.91 (± 25.21)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 24

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 24[29]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1398	450		
Units: IU/L				
arithmetic mean (standard deviation)				
AST (n =1397, 450)	4.1 (± 14.64)	6.77 (± 15.74)		
ALT (n =1398, 450)	5.31 (± 19.37)	7.56 (± 18.93)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 36

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 36[30]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1122	384		
Units: IU/L				
arithmetic mean (standard deviation)				
AST	5.38 (± 20.68)	5.32 (± 15.65)		
ALT	5.46 (± 20.61)	6.56 (± 22.43)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 48

End point title	Change From Baseline in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Levels at Month 48[31]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	417	127		
Units: IU/L				
arithmetic mean (standard deviation)				
AST (n =416, 127)	4.49 (± 14.05)	8.4 (± 26.41)		
ALT (n =417, 127)	4.92 (± 27.11)	6.92 (± 20.98)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change From Baseline in Physical Examination

End point title	Number of Subjects With Clinically Significant Change From Baseline in Physical Examination[32]

End point description:

Physical examinations included: general appearance; skin, head, eyes, ears, nose and throat; heart; lungs; abdomen; lower extremities (for the presence of peripheral edema) and lymph nodes. Clinical significance of change from baseline values in physical examination was based on investigator's discretion. Safety analysis set. Here, 'N' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2268	577		
Units: subjects	683	191		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Vital Sign Abnormalities

End point title	Number of Subjects With Vital Sign Abnormalities[33]

End point description:

Criteria for abnormalities in vital signs included: Systolic blood pressure (SBP): less than (<) 90 millimeter of mercury (mmHg); diastolic blood pressure (DBP): <50 and greater than (>) 120 mmHg; heart rate: <40 and >120 beats per minute (BPM); SBP values: maximum increase from baseline (IFB) of greater than or equal to (>=) 30 mmHg; DBP value: maximum IFB of >=20 mmHg. Safety analysis set. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2271	577		
Units: subjects				
Systolic BP (n =2271, 577)	12	6		
Diastolic BP (n =2271, 577)	12	1		
Heart Rate (n =2271, 577)	3	1		
Maximum IFB in Systolic BP (n =2267, 577)	187	65		
Maximum IFB in Diastolic BP (n =2267, 577)	221	74		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 1

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 1[34]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2277	586		
Units: millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
Baseline: Systolic BP (n =2277, 586)	126.07 (± 14.03)	126.24 (± 14.12)		
Baseline: Diastolic BP (n =2277, 586)	79.64 (± 9.42)	78.88 (± 9.27)		
Change at Month 1: Systolic BP (n =2210, 564)	-0.43 (± 11.83)	-1.31 (± 11.55)		
Change at Month 1: Diastolic BP (n =2210, 564)	-0.03 (± 8.42)	0.22 (± 8.45)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 3

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 3[35]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2214	575		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	-0.16 (± 11.97)	-0.95 (± 11.85)		
Diastolic BP	-0.26 (± 8.56)	0.05 (± 8.52)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 6

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 6[36]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2061	566		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	0.22 (± 12.18)	-0.15 (± 12.48)		
Diastolic BP	-0.05 (± 8.87)	0.55 (± 8.74)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 12

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 12[37]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1784	534		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	0.42 (± 11.97)	-0.2 (± 12.51)		
Diastolic BP	0.23 (± 8.89)	0.1 (± 9.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 24

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 24[38]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[38] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1398	451		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	0.84 (± 13)	-0.07 (± 13.02)		
Diastolic BP	0.36 (± 9.45)	0.35 (± 8.85)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 36

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 36[39]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1123	386		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	0.52 (± 13.15)	0.1 (± 13.92)		
Diastolic BP	0.33 (± 9.33)	-0.06 (± 9.24)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 48

End point title	Change From Baseline in Systolic Blood Pressure (BP) and Diastolic BP at Month 48[40]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	422	127		
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic BP	2.35 (± 13.45)	1.13 (± 15.18)		
Diastolic BP	0.97 (± 9.52)	0.87 (± 9.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 1

End point title	Change From Baseline in Heart Rate at Month 1[41]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 1

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2277	586		
Units: beats per minute				
arithmetic mean (standard deviation)				
Baseline (n =2277, 586)	71.81 (± 9.67)	71.46 (± 9.93)		
Change at Month 1 (n =2210, 563)	-0.82 (± 9.16)	-1.23 (± 9.03)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 3

End point title	Change From Baseline in Heart Rate at Month 3[42]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of

subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 3

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2214	573		
Units: beats per minute				
arithmetic mean (standard deviation)	-0.57 (± 9.35)	-0.32 (± 9.19)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 6

End point title	Change From Baseline in Heart Rate at Month 6[43]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2061	565		
Units: beats per minute				
arithmetic mean (standard deviation)	-0.73 (± 9.65)	-1.05 (± 9.18)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 12

End point title	Change From Baseline in Heart Rate at Month 12[44]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[44] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1784	534		
Units: beats per minute				
arithmetic mean (standard deviation)	-1.13 (± 9.66)	-1.14 (± 9.07)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 24

End point title	Change From Baseline in Heart Rate at Month 24[45]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[45] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1398	451		
Units: beats per minute				
arithmetic mean (standard deviation)	-1.07 (± 9.91)	-0.94 (± 8.89)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 36

End point title	Change From Baseline in Heart Rate at Month 36[46]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1123	386		
Units: beats per minute				
arithmetic mean (standard deviation)	-1.38 (± 9.81)	-1 (± 9.26)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Heart Rate at Month 48

End point title	Change From Baseline in Heart Rate at Month 48[47]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[47] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	422	127		
Units: beats per minute				
arithmetic mean (standard deviation)	-0.91 (± 10.64)	-0.64 (± 10.64)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Electrocardiogram (ECG) Abnormalities

End point title	Number of Subjects With Electrocardiogram (ECG) Abnormalities[48]

End point description:

Criteria for ECG abnormality: PR interval >=300 milliseconds (msec); QT interval >=500 msec; QTcB (Bazett's Correction) and QTcF (Fridericia's Correction) 450 to <480 msec, 480 to <500 msec and >=500 msec. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[48] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: subjects	7	2		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 6

End point title	Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 6[49]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 6

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2264	583		
Units: milliseconds (msec)				
arithmetic mean (standard deviation)				
Baseline: QRS Complex (n =2264, 583)	92.88 (± 9.12)	92.31 (± 9.75)		
Baseline: PR Interval (n =2258, 583)	162.32 (± 21.32)	158.91 (± 20.62)		
Baseline: QT Interval (n =2264, 583)	392.39 (± 29.12)	395.75 (± 29.7)		
Baseline: QTcB Interval (n =2264, 583)	415.7 (± 23.83)	416.91 (± 23.04)		
Baseline: QTcF Interval (n =2264, 583)	407.48 (± 20.74)	409.42 (± 20.11)		
Baseline: RR Interval (n =2264, 583)	901.27 (± 145.58)	911.59 (± 150.35)		
Change at Month 6: QRS Complex (n =1995, 550)	1.51 (± 8.28)	2.01 (± 7.5)		

Change at Month 6: PR Interval (n =1986, 549)	2.46 (± 13.79)	2.76 (± 14.81)		
Change at Month 6: QT Interval (n =1995, 550)	2.25 (± 24.49)	2.52 (± 24.39)		
Change at Month 6: QTcB Interval (n =1995, 550)	-0.84 (± 20.49)	-1.38 (± 20.31)		
Change at Month 6: QTcF Interval (n =1995, 550)	0.23 (± 17.14)	-0.03 (± 17.68)		
Change at Month 6: RR Interval (n =1995, 550)	14.35 (± 130.91)	18.77 (± 123.49)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 12

End point title	Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 12[50]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[50] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1727	516		
Units: msec				
arithmetic mean (standard deviation)				
QRS Complex (n =1726, 516)	1.89 (± 7.93)	2.11 (± 7.53)		
PR Interval (n =1717, 515)	2.8 (± 14.32)	3.21 (± 14.31)		
QT Interval (n =1726, 516)	2.49 (± 23.26)	2.69 (± 23)		
QTcB Interval (n =1726, 516)	-1.04 (± 20.63)	-1.09 (± 20.83)		
QTcF Interval (n =1726, 516)	0.16 (± 16.71)	0.23 (± 17.2)		
RR Interval (n =1727, 516)	15.94 (± 130.6)	17.55 (± 128.16)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval

at Month 24

End point title	Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 24[51]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 24

Notes:

[51] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1352	432		
Units: msec				
arithmetic mean (standard deviation)				
QRS Complex (n =1352, 432)	2 (± 8.55)	2.42 (± 9.13)		
PR Interval (n =1346, 432)	3.49 (± 14.55)	3.81 (± 14.67)		
QT Interval (n =1352, 432)	3.93 (± 24.93)	2.28 (± 24.8)		
QTcB Interval (n =1352, 431)	0.15 (± 20.77)	0.78 (± 21.06)		
QTcF Interval (n =1352, 431)	1.47 (± 16.86)	1.25 (± 17.72)		
RR Interval (n =1352, 432)	17.7 (± 139.47)	8.66 (± 135.06)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 36

End point title	Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 36[52]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 36

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	845	283		
Units: msec				
arithmetic mean (standard deviation)				
QRS Complex (n =845, 283)	1.75 (± 8.47)	1.85 (± 10.37)		
PR Interval (n =840, 282)	4.18 (± 14.5)	3.25 (± 15.5)		
QT Interval (n =844, 283)	4.31 (± 24.93)	2.52 (± 22.63)		
QTcB Interval (n =844, 283)	0.44 (± 21.29)	-0.01 (± 22.21)		
QTcF Interval (n =844, 283)	1.79 (± 17.57)	0.84 (± 17.63)		
RR Interval (n =845, 283)	18.24 (± 136.44)	15.14 (± 131.42)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 48

End point title	Change From Baseline in QRS Complex, PR, QT, QTcB, QTcF and RR Interval at Month 48[53]

End point description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Here, 'number of subjects analyzed' signifies subjects evaluable for this endpoint and ‘n’ signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Primary

End point timeframe:

Baseline, Month 48

Notes:

[53] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	55		
Units: msec				
arithmetic mean (standard deviation)				
QRS Complex (n =126, 55)	2.37 (± 10.17)	1.31 (± 5.37)		
PR Interval (n =126, 55)	6.26 (± 12.58)	1.98 (± 13.2)		
QT Interval (n =126, 55)	6.43 (± 24.05)	1.69 (± 23.43)		
QTcB Interval (n =125, 55)	3.42 (± 20.11)	-2 (± 22.64)		
QTcF Interval (n =125, 55)	4.55 (± 15.84)	-0.87 (± 19.38)		
RR Interval (n =126, 55)	15.69 (± 143.06)	20.78 (± 119.61)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adjudicated Cardiovascular Events

End point title	Number of Subjects With Adjudicated Cardiovascular Events[54]

End point description:

Adjudicated cardiovascular events were assessed by adjudication committee as independent reviewers based on event documentation including: hospital discharge summaries, operative reports, clinic notes, ECGs, diagnostic enzymes, results of other diagnostic tests, autopsy reports and death certificate information; as applicable. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[54] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: subjects	32	13		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Malignancy Events

End point title	Number of Subjects With Malignancy Events[55]

End point description:

Malignancy events included lymphoma, and demyelinating neurologic events. Biopsies collected for malignancy events were submitted to the central laboratory for pathologist over-read. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Notes:

[55] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: subjects	87	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Physician Global Assessment (PGA) Response of 'Clear' or 'Almost Clear'

End point title	Percentage of Subjects Achieving Physician Global Assessment (PGA) Response of 'Clear' or 'Almost Clear'

End point description:

PGA of psoriasis was scored on a 5-point scale,reflecting a global consideration of the erythema (E),induration (I) and scaling (S) across all psoriatic lesions in subjects.The severity rating scores(Erythema: 0= no evidence of erythema to 4= dark, deep red; Induration: 0= no evidence of plaque elevation to 4= marked plaque elevation, hard/sharp borders;Scaling: 0= no evidence of scaling to 4= thick, coarse scale predominates) were summed (E + I + S= total) and the average (total/3) was taken. Total average was rounded to the nearest whole number score to determine the PGA.The 5-point scale for PGA was: 0= clear;1= almost clear;2= mild;3= moderate;4= severe,where higher score indicating more severity.Percentage of subjects with response of 'clear' (score of '0') and 'almost clear' (score of '1') were reported. Full analysis set (FAS).Here,'number of subjects analyzed' =subjects evaluable for this endpoint and 'n'=subjects evaluable at specified time points for each arm,

End point type	Secondary

End point timeframe:

Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2200	571		
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =2196, 563)	50.36 (48.27 to 52.46)	77.8 (74.36 to 81.23)		
Month 3 (n =2200, 571)	54.86 (52.78 to 56.94)	85.29 (82.38 to 88.19)		
Month 6 (n =2052, 564)	54.97 (52.82 to 57.12)	82.09 (78.93 to 85.26)		
Month 12 (n =1776, 532)	54.79 (52.47 to 57.1)	75.19 (71.52 to 78.86)		
Month 24 (n =1397, 448)	54.62 (52.01 to 57.23)	79.46 (75.72 to 83.2)		
Month 36 (n =1123, 385)	57.35 (54.45 to 60.24)	76.36 (72.12 to 80.61)		
Month 48 (n =422, 126)	48.58 (43.81 to 53.35)	77.78 (70.52 to 85.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Greater Than or Equal to (>=) 75 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point title	Percentage of Subjects Achieving Greater Than or Equal to (>=) 75 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease),with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. Percentage of subjects with >=75% reduction from baseline in PASI scores were reported. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2200	566		
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =2194, 555)	51.96 (49.87 to 54.05)	71.89 (68.15 to 75.63)		
Month 3 (n =2200, 566)	58.45 (56.4 to 60.51)	84.45 (81.47 to 87.44)		
Month 6 (n =2048, 557)	61.67 (59.56 to 63.78)	86 (83.11 to 88.88)		
Month 12 (n =1775, 525)	65.24 (63.02 to 67.45)	80.76 (77.39 to 84.13)		
Month 24 (n =1393, 445)	67.26 (64.8 to 69.73)	84.94 (81.62 to 88.27)		
Month 36 (n =1118, 380)	70.75 (68.08 to 73.42)	83.95 (80.26 to 87.64)		
Month 48 (n =422, 124)	64.93 (60.38 to 69.48)	83.06 (76.46 to 89.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Area and Severity Index (PASI) Scores

End point title	Psoriasis Area and Severity Index (PASI) Scores

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2266	585		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2266, 585)	21.85 (± 9.48)	19.05 (± 8.89)		
Month 1 (n =2198, 561)	6.6 (± 7.14)	3.09 (± 4.81)		
Month 3 (n =2205, 572)	5.64 (± 6.33)	1.95 (± 3.25)		
Month 6 (n =2051, 563)	5.31 (± 6.31)	1.9 (± 3.25)		
Month 12 (n =1779, 531)	4.72 (± 5.29)	2.38 (± 3.57)		
Month 24 (n =1397, 449)	4.41 (± 5.08)	1.9 (± 2.65)		
Month 36 (n =1121, 384)	3.91 (± 4.66)	2.19 (± 3.23)		
Month 48 (n =422, 126)	4.75 (± 5.37)	1.85 (± 2.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriasis Area and Severity Index (PASI) Scores at Month 1, 3, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Psoriasis Area and Severity Index (PASI) Scores at Month 1, 3, 6, 12, 24, 36 and 48

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. FAS. Here, ‘number of subjects analyzed’= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2201	572		
Units: units on a scale				
arithmetic mean (standard deviation)				

Month 1 (n =2195, 561)	-15.26 (± 9.96)	-16 (± 9.57)		
Month 3 (n =2201, 572)	-16.18 (± 9.73)	-16.99 (± 9.27)		
Month 6 (n =2049, 563)	-16.56 (± 9.54)	-17.03 (± 9.16)		
Month 12 (n =1776, 531)	-17.01 (± 9.33)	-16.45 (± 9.04)		
Month 24 (n =1394, 449)	-17.25 (± 9.35)	-16.67 (± 8.7)		
Month 36 (n =1119, 384)	-17.44 (± 9.23)	-16.49 (± 8.81)		
Month 48 (n =422, 126)	-16.16 (± 8.61)	-15.47 (± 9.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Area and Severity Index (PASI) Component Scores: Erythema

End point title	Psoriasis Area and Severity Index (PASI) Component Scores: Erythema

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Erythema was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2266	585		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Head/Neck (n =2266, 585)	2.26 (± 0.99)	2.13 (± 1.08)		
Month 1: Head/Neck (n =2198, 561)	0.82 (± 0.96)	0.47 (± 0.81)		
Month 3: Head/Neck (n =2205, 572)	0.76 (± 0.95)	0.34 (± 0.65)		
Month 6: Head/Neck (n =2051, 563)	0.75 (± 0.95)	0.42 (± 0.75)		
Month 12: Head/Neck (n =1779, 531)	0.7 (± 0.92)	0.49 (± 0.82)		
Month 24: Head/Neck (n =1397, 449)	0.66 (± 0.93)	0.47 (± 0.75)		
Month 36: Head/Neck (n =1121, 384)	0.57 (± 0.88)	0.48 (± 0.79)		
Month 48: Head/Neck (n =422, 126)	0.7 (± 0.93)	0.34 (± 0.69)		
Baseline: Upper Limbs (n =2266, 585)	2.82 (± 0.74)	2.68 (± 0.86)		
Month 1: Upper Limbs (n =2198, 561)	1.29 (± 0.98)	0.71 (± 0.86)		
Month 3: Upper Limbs (n =2205, 572)	1.23 (± 1)	0.57 (± 0.79)		

Month 6: Upper Limbs (n =2051, 563)	1.2 (± 1.01)	0.58 (± 0.83)		
Month 12: Upper Limbs (n =1779, 531)	1.16 (± 1.01)	0.74 (± 0.95)		
Month 24: Upper Limbs (n =1397, 449)	1.13 (± 1.03)	0.61 (± 0.85)		
Month 36: Upper Limbs (n =1121, 384)	1.06 (± 1.01)	0.68 (± 0.86)		
Month 48: Upper Limbs (n =422, 126)	1.18 (± 1.03)	0.58 (± 0.84)		
Baseline: Trunk (n =2266, 585)	2.83 (± 0.83)	2.73 (± 0.94)		
Month 1: Trunk (n =2198, 561)	1.18 (± 1.11)	0.62 (± 0.92)		
Month 3: Trunk (n =2205, 572)	1.06 (± 1.09)	0.41 (± 0.73)		
Month 6: Trunk (n =2051, 563)	1.03 (± 1.09)	0.41 (± 0.79)		
Month 12: Trunk (n =1779, 531)	0.99 (± 1.08)	0.51 (± 0.89)		
Month 24: Trunk (n =1397, 449)	0.96 (± 1.08)	0.49 (± 0.84)		
Month 36: Trunk (n =1121, 384)	0.86 (± 1.06)	0.53 (± 0.9)		
Month 48: Trunk (n =422, 126)	1 (± 1.1)	0.5 (± 0.86)		
Baseline: Lower Limbs (n =2266, 585)	3.1 (± 0.7)	2.94 (± 0.89)		
Month 1: Lower Limbs (n =2198, 561)	1.37 (± 1.09)	0.79 (± 0.95)		
Month 3: Lower Limbs (n =2205, 572)	1.24 (± 1.08)	0.58 (± 0.84)		
Month 6: Lower Limbs (n =2051, 563)	1.2 (± 1.11)	0.52 (± 0.81)		
Month 12: Lower Limbs (n =1779, 531)	1.17 (± 1.1)	0.69 (± 0.98)		
Month 24: Lower Limbs (n =1397, 449)	1.15 (± 1.11)	0.59 (± 0.9)		
Month 36: Lower Limbs (n =1121, 384)	1.07 (± 1.11)	0.67 (± 0.96)		
Month 48: Lower Limbs (n =422, 126)	1.2 (± 1.11)	0.61 (± 0.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Area and Severity Index (PASI) Component Scores: Induration

End point title	Psoriasis Area and Severity Index (PASI) Component Scores: Induration

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Induration was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2266	585		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Head/Neck (n =2266, 585)	1.97 (± 1.01)	1.88 (± 1.1)		
Month 1: Head/Neck (n =2198, 561)	0.65 (± 0.85)	0.35 (± 0.73)		

Month 3: Head/Neck (n =2205, 572)	0.6 (± 0.84)	0.26 (± 0.56)		
Month 6: Head/Neck (n =2051, 563)	0.59 (± 0.86)	0.31 (± 0.67)		
Month 12: Head/Neck (n =1779, 531)	0.55 (± 0.81)	0.38 (± 0.71)		
Month 24: Head/Neck (n =1397, 449)	0.53 (± 0.82)	0.37 (± 0.68)		
Month 36: Head/Neck (n =1121, 384)	0.46 (± 0.77)	0.37 (± 0.68)		
Month 48: Head/Neck (n =422, 126)	0.6 (± 0.85)	0.26 (± 0.6)		
Baseline: Upper Limbs (n =2266, 585)	2.64 (± 0.77)	2.5 (± 0.93)		
Month 1: Upper Limbs (n =2198, 561)	1.21 (± 0.99)	0.66 (± 0.88)		
Month 3: Upper Limbs (n =2205, 572)	1.17 (± 1.01)	0.53 (± 0.81)		
Month 6: Upper Limbs (n =2051, 563)	1.15 (± 1.02)	0.55 (± 0.85)		
Month 12: Upper Limbs (n =1779, 531)	1.11 (± 1.01)	0.69 (± 0.95)		
Month 24: Upper Limbs (n =1397, 449)	1.08 (± 1.02)	0.53 (± 0.84)		
Month 36: Upper Limbs (n =1121, 384)	1 (± 1.01)	0.6 (± 0.82)		
Month 48: Upper Limbs (n =422, 126)	1.09 (± 1)	0.5 (± 0.75)		
Baseline: Trunk (n =2266, 585)	2.57 (± 0.86)	2.51 (± 1.01)		
Month 1: Trunk (n =2198, 561)	1.02 (± 1.04)	0.52 (± 0.86)		
Month 3: Trunk (n =2205, 572)	0.91 (± 1.02)	0.34 (± 0.68)		
Month 6: Trunk (n =2051, 563)	0.88 (± 1)	0.34 (± 0.71)		
Month 12: Trunk (n =1779, 531)	0.87 (± 1)	0.42 (± 0.77)		
Month 24: Trunk (n =1397, 449)	0.82 (± 0.98)	0.39 (± 0.73)		
Month 36: Trunk (n =1121, 384)	0.75 (± 0.97)	0.43 (± 0.79)		
Month 48: Trunk (n =422, 126)	0.91 (± 1.05)	0.44 (± 0.8)		
Baseline: Lower Limbs (n =2266, 585)	2.85 (± 0.76)	2.77 (± 0.96)		
Month 1: Lower Limbs (n =2198, 561)	1.22 (± 1.04)	0.68 (± 0.95)		
Month 3: Lower Limbs (n =2205, 572)	1.1 (± 1.04)	0.51 (± 0.84)		
Month 6: Lower Limbs (n =2051, 563)	1.08 (± 1.06)	0.47 (± 0.82)		
Month 12: Lower Limbs (n =1779, 531)	1.05 (± 1.03)	0.61 (± 0.94)		
Month 24: Lower Limbs (n =1397, 449)	1.02 (± 1.03)	0.49 (± 0.83)		
Month 36: Lower Limbs (n =1121, 384)	0.95 (± 1.03)	0.57 (± 0.87)		
Month 48: Lower Limbs (n =422, 126)	1.07 (± 1.04)	0.48 (± 0.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriasis Area and Severity Index (PASI) Component Scores: Scaling

End point title	Psoriasis Area and Severity Index (PASI) Component Scores: Scaling

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Scaling was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2266	585		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Head/Neck (n =2266, 585)	2.22 (± 1.08)	2.1 (± 1.11)		
Month 1: Head/Neck (n =2198, 561)	0.75 (± 0.95)	0.42 (± 0.79)		
Month 3: Head/Neck (n =2205, 572)	0.71 (± 0.95)	0.32 (± 0.66)		
Month 6: Head/Neck (n =2051, 563)	0.71 (± 0.97)	0.4 (± 0.77)		
Month 12: Head/Neck (n =1779, 531)	0.67 (± 0.92)	0.48 (± 0.84)		
Month 24: Head/Neck (n =1397, 449)	0.6 (± 0.88)	0.45 (± 0.77)		
Month 36: Head/Neck (n =1121, 384)	0.55 (± 0.88)	0.47 (± 0.79)		
Month 48: Head/Neck (n =422, 126)	0.65 (± 0.93)	0.34 (± 0.72)		
Baseline: Upper Limbs (n =2266, 585)	2.65 (± 0.82)	2.52 (± 0.96)		
Month 1: Upper Limbs (n =2198, 561)	1.22 (± 1.01)	0.69 (± 0.89)		
Month 3: Upper Limbs (n =2205, 572)	1.18 (± 1.04)	0.55 (± 0.8)		
Month 6: Upper Limbs (n =2051, 563)	1.16 (± 1.05)	0.58 (± 0.87)		
Month 12: Upper Limbs (n =1779, 531)	1.12 (± 1.03)	0.72 (± 0.97)		
Month 24: Upper Limbs (n =1397, 449)	1.08 (± 1.03)	0.58 (± 0.84)		
Month 36: Upper Limbs (n =1121, 384)	1.01 (± 1.02)	0.62 (± 0.83)		
Month 48: Upper Limbs (n =422, 126)	1.13 (± 1.09)	0.53 (± 0.79)		
Baseline: Trunk (n =2266, 585)	2.55 (± 0.89)	2.47 (± 1)		
Month 1: Trunk (n =2198, 561)	0.97 (± 1.02)	0.5 (± 0.83)		
Month 3: Trunk (n =2205, 572)	0.87 (± 1)	0.33 (± 0.64)		
Month 6: Trunk (n =2051, 563)	0.85 (± 0.99)	0.33 (± 0.7)		
Month 12: Trunk (n =1779, 531)	0.83 (± 0.97)	0.4 (± 0.76)		
Month 24: Trunk (n =1397, 449)	0.78 (± 0.95)	0.39 (± 0.72)		
Month 36: Trunk (n =1121, 384)	0.71 (± 0.93)	0.42 (± 0.77)		
Month 48: Trunk (n =422, 126)	0.86 (± 0.99)	0.4 (± 0.78)		
Baseline: Lower Limbs (n =2266, 585)	2.89 (± 0.81)	2.79 (± 1)		
Month 1: Lower Limbs (n =2198, 561)	1.23 (± 1.08)	0.7 (± 0.93)		
Month 3: Lower Limbs (n =2205, 572)	1.12 (± 1.08)	0.48 (± 0.78)		
Month 6: Lower Limbs (n =2051, 563)	1.11 (± 1.1)	0.48 (± 0.83)		
Month 12: Lower Limbs (n =1779, 531)	1.07 (± 1.07)	0.64 (± 0.98)		
Month 24: Lower Limbs (n =1397, 449)	1.04 (± 1.06)	0.53 (± 0.84)		
Month 36: Lower Limbs (n =1121, 384)	0.94 (± 1.03)	0.6 (± 0.9)		
Month 48: Lower Limbs (n =422, 126)	1.09 (± 1.09)	0.48 (± 0.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriasis Area and Severity Index (PASI) Component Scores: Erythema at Month 1, 3, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Psoriasis Area and Severity Index

	(PASI) Component Scores: Erythema at Month 1, 3, 6, 12, 24, 36 and 48

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Erythema was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2201	572		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1: Head/Neck (n =2195, 561)	-1.43 (± 1.15)	-1.66 (± 1.2)		
Month 3: Head/Neck (n =2201, 572)	-1.5 (± 1.18)	-1.8 (± 1.18)		
Month 6: Head/Neck (n =2049, 563)	-1.52 (± 1.2)	-1.72 (± 1.21)		
Month 12: Head/Neck (n =1776, 531)	-1.56 (± 1.19)	-1.64 (± 1.22)		
Month 24: Head/Neck (n =1394, 449)	-1.62 (± 1.19)	-1.67 (± 1.23)		
Month 36: Head/Neck (n =1119, 384)	-1.72 (± 1.18)	-1.67 (± 1.2)		
Month 48: Head/Neck (n =422, 126)	-1.55 (± 1.19)	-1.7 (± 1.13)		
Month 1: Upper Limbs (n =2195, 561)	-1.53 (± 1.12)	-1.98 (± 1.18)		
Month 3: Upper Limbs (n =2201, 572)	-1.59 (± 1.15)	-2.12 (± 1.14)		
Month 6: Upper Limbs (n =2049, 563)	-1.62 (± 1.15)	-2.09 (± 1.13)		
Month 12: Upper Limbs (n =1776, 531)	-1.67 (± 1.15)	-1.94 (± 1.21)		
Month 24: Upper Limbs (n =1394, 449)	-1.7 (± 1.18)	-2.05 (± 1.19)		
Month 36: Upper Limbs (n =1119, 384)	-1.78 (± 1.17)	-2 (± 1.18)		
Month 48: Upper Limbs (n =422, 126)	-1.62 (± 1.16)	-1.9 (± 1.22)		
Month 1: Trunk (n =2195, 561)	-1.65 (± 1.22)	-2.12 (± 1.26)		
Month 3: Trunk (n =2201, 572)	-1.77 (± 1.24)	-2.33 (± 1.17)		
Month 6: Trunk (n =2049, 563)	-1.81 (± 1.24)	-2.32 (± 1.19)		
Month 12: Trunk (n =1776, 531)	-1.86 (± 1.24)	-2.21 (± 1.25)		
Month 24: Trunk (n =1394, 449)	-1.88 (± 1.25)	-2.22 (± 1.26)		
Month 36: Trunk (n =1119, 384)	-1.99 (± 1.26)	-2.18 (± 1.3)		
Month 48: Trunk (n =422, 126)	-1.82 (± 1.22)	-2.08 (± 1.17)		
Month 1: Lower Limbs (n =2195, 561)	-1.72 (± 1.19)	-2.16 (± 1.26)		
Month 3: Lower Limbs (n =2201, 572)	-1.87 (± 1.21)	-2.36 (± 1.21)		
Month 6: Lower Limbs (n =2049, 563)	-1.9 (± 1.22)	-2.42 (± 1.18)		
Month 12: Lower Limbs (n =1776, 531)	-1.94 (± 1.23)	-2.24 (± 1.33)		
Month 24: Lower Limbs (n =1394, 449)	-1.95 (± 1.25)	-2.32 (± 1.24)		
Month 36: Lower Limbs (n =1119, 384)	-2.04 (± 1.23)	-2.28 (± 1.3)		
Month 48: Lower Limbs (n =422, 126)	-1.87 (± 1.2)	-2.17 (± 1.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriasis Area and Severity Index (PASI) Component Scores: Induration at Month 1, 3, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Psoriasis Area and Severity Index (PASI) Component Scores: Induration at Month 1, 3, 6, 12, 24, 36 and 48

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Induration was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2201	572		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1: Head/Neck (n =2195, 561)	-1.32 (± 1.13)	-1.53 (± 1.15)		
Month 3: Head/Neck (n =2201, 572)	-1.37 (± 1.17)	-1.63 (± 1.14)		
Month 6: Head/Neck (n =2049, 563)	-1.4 (± 1.16)	-1.57 (± 1.18)		
Month 12: Head/Neck (n =1776, 531)	-1.44 (± 1.18)	-1.49 (± 1.18)		
Month 24: Head/Neck (n =1394, 449)	-1.48 (± 1.17)	-1.51 (± 1.21)		
Month 36: Head/Neck (n =1119, 384)	-1.55 (± 1.17)	-1.51 (± 1.15)		
Month 48: Head/Neck (n =422, 126)	-1.35 (± 1.17)	-1.41 (± 1.1)		
Month 1: Upper Limbs (n =2195, 561)	-1.43 (± 1.14)	-1.85 (± 1.22)		
Month 3: Upper Limbs (n =2201, 572)	-1.47 (± 1.17)	-1.97 (± 1.16)		
Month 6: Upper Limbs (n =2049, 563)	-1.49 (± 1.15)	-1.94 (± 1.19)		
Month 12: Upper Limbs (n =1776, 531)	-1.54 (± 1.14)	-1.82 (± 1.27)		
Month 24: Upper Limbs (n =1394, 449)	-1.57 (± 1.18)	-1.97 (± 1.19)		
Month 36: Upper Limbs (n =1119, 384)	-1.65 (± 1.17)	-1.92 (± 1.18)		
Month 48: Upper Limbs (n =422, 126)	-1.53 (± 1.14)	-1.83 (± 1.14)		
Month 1: Trunk (n =2195, 561)	-1.55 (± 1.19)	-2.01 (± 1.26)		
Month 3: Trunk (n =2201, 572)	-1.65 (± 1.22)	-2.17 (± 1.18)		
Month 6: Trunk (n =2049, 563)	-1.7 (± 1.19)	-2.18 (± 1.2)		
Month 12: Trunk (n =1776, 531)	-1.71 (± 1.2)	-2.1 (± 1.24)		
Month 24: Trunk (n =1394, 449)	-1.76 (± 1.19)	-2.13 (± 1.2)		
Month 36: Trunk (n =1119, 384)	-1.85 (± 1.2)	-2.09 (± 1.23)		
Month 48: Trunk (n =422, 126)	-1.68 (± 1.17)	-1.87 (± 1.2)		
Month 1: Lower Limbs (n =2195, 561)	-1.63 (± 1.22)	-2.09 (± 1.31)		
Month 3: Lower Limbs (n =2201, 572)	-1.75 (± 1.22)	-2.26 (± 1.24)		
Month 6: Lower Limbs (n =2049, 563)	-1.78 (± 1.23)	-2.3 (± 1.23)		
Month 12: Lower Limbs (n =1776, 531)	-1.82 (± 1.2)	-2.17 (± 1.33)		

Month 24: Lower Limbs (n =1394, 449)	-1.85 (± 1.22)	-2.28 (± 1.24)		
Month 36: Lower Limbs (n =1119, 384)	-1.93 (± 1.21)	-2.22 (± 1.29)		
Month 48: Lower Limbs (n =422, 126)	-1.77 (± 1.18)	-2.07 (± 1.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Psoriasis Area and Severity Index (PASI) Component Scores: Scaling at Month 1, 3, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Psoriasis Area and Severity Index (PASI) Component Scores: Scaling at Month 1, 3, 6, 12, 24, 36 and 48

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Scaling was assessed separately for four body areas (head and neck, upper limbs, trunk and lower limbs) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2201	572		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1: Head/Neck (n =2195, 561)	-1.46 (± 1.19)	-1.69 (± 1.2)		
Month 3: Head/Neck (n =2201, 572)	-1.51 (± 1.24)	-1.78 (± 1.19)		
Month 6: Head/Neck (n =2049, 563)	-1.52 (± 1.24)	-1.7 (± 1.22)		
Month 12: Head/Neck (n =1776, 531)	-1.56 (± 1.25)	-1.61 (± 1.24)		
Month 24: Head/Neck (n =1394, 449)	-1.63 (± 1.24)	-1.63 (± 1.27)		
Month 36: Head/Neck (n =1119, 384)	-1.68 (± 1.22)	-1.64 (± 1.22)		
Month 48: Head/Neck (n =422, 126)	-1.53 (± 1.24)	-1.58 (± 1.17)		
Month 1: Upper Limbs (n =2195, 561)	-1.44 (± 1.18)	-1.84 (± 1.24)		
Month 3: Upper Limbs (n =2201, 572)	-1.47 (± 1.2)	-1.97 (± 1.18)		
Month 6: Upper Limbs (n =2049, 563)	-1.49 (± 1.21)	-1.94 (± 1.26)		
Month 12: Upper Limbs (n =1776, 531)	-1.52 (± 1.21)	-1.82 (± 1.3)		
Month 24: Upper Limbs (n =1394, 449)	-1.56 (± 1.22)	-1.96 (± 1.22)		
Month 36: Upper Limbs (n =1119, 384)	-1.65 (± 1.19)	-1.93 (± 1.15)		
Month 48: Upper Limbs (n =422, 126)	-1.45 (± 1.19)	-1.78 (± 1.22)		
Month 1: Trunk (n =2195, 561)	-1.58 (± 1.2)	-1.98 (± 1.24)		
Month 3: Trunk (n =2201, 572)	-1.67 (± 1.22)	-2.14 (± 1.14)		
Month 6: Trunk (n =2049, 563)	-1.7 (± 1.19)	-2.14 (± 1.22)		
Month 12: Trunk (n =1776, 531)	-1.72 (± 1.21)	-2.08 (± 1.23)		
Month 24: Trunk (n =1394, 449)	-1.77 (± 1.2)	-2.11 (± 1.19)		

Month 36: Trunk (n =1119, 384)	-1.84 (± 1.2)	-2.06 (± 1.23)		
Month 48: Trunk (n =422, 126)	-1.62 (± 1.19)	-1.8 (± 1.18)		
Month 1: Lower Limbs (n =2195, 561)	-1.67 (± 1.24)	-2.09 (± 1.3)		
Month 3: Lower Limbs (n =2201, 572)	-1.77 (± 1.26)	-2.3 (± 1.23)		
Month 6: Lower Limbs (n =2049, 563)	-1.79 (± 1.27)	-2.3 (± 1.25)		
Month 12: Lower Limbs (n =1776, 531)	-1.83 (± 1.26)	-2.15 (± 1.36)		
Month 24: Lower Limbs (n =1394, 449)	-1.86 (± 1.27)	-2.25 (± 1.24)		
Month 36: Lower Limbs (n =1119, 384)	-1.97 (± 1.23)	-2.21 (± 1.26)		
Month 48: Lower Limbs (n =422, 126)	-1.77 (± 1.29)	-2.11 (± 1.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Greater Than or Equal to (>=) 50 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point title	Percentage of Subjects Achieving Greater Than or Equal to (>=) 50 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. Percentage of subjects with >=50% reduction from baseline in PASI scores were reported. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2200	566		
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =2194, 555)	76.53 (74.75 to 78.3)	86.67 (83.84 to 89.49)		
Month 3 (n =2200, 566)	81.59 (79.97 to 83.21)	95.05 (93.27 to 96.84)		
Month 6 (n =2048, 557)	85.64 (84.13 to 87.16)	93.9 (91.91 to 95.88)		
Month 12 (n =1775, 525)	87.66 (86.13 to 89.19)	93.14 (90.98 to 95.3)		
Month 24 (n =1393, 445)	88.87 (87.22 to 90.52)	94.61 (92.51 to 96.71)		
Month 36 (n =1118, 380)	90.97 (89.29 to 92.65)	92.63 (90 to 95.26)		

Month 48 (n =422, 124)	88.86 (85.86 to 91.86)	97.58 (94.88 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Greater Than or Equal to (>=) 90 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point title	Percentage of Subjects Achieving Greater Than or Equal to (>=) 90 Percent Reduction From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. Percentage of subjects with >=90% reduction from baseline in PASI scores were reported. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2200	566		
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =2194, 555)	29.99 (28.07 to 31.91)	56.04 (51.91 to 60.17)		
Month 3 (n =2200, 566)	33.73 (31.75 to 35.7)	65.37 (61.45 to 69.29)		
Month 6 (n =2048, 557)	35.21 (33.14 to 37.27)	65.89 (61.95 to 69.83)		
Month 12 (n =1775, 525)	35.94 (33.71 to 38.18)	61.71 (57.56 to 65.87)		
Month 24 (n =1393, 445)	38.33 (35.78 to 40.89)	62.02 (57.51 to 66.53)		
Month 36 (n =1118, 380)	43.02 (40.12 to 45.93)	60.53 (55.61 to 65.44)		
Month 48 (n =422, 124)	34.36 (29.83 to 38.89)	58.06 (49.38 to 66.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Greater Than or Equal to (>=) 125 Percent Increase From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point title	Percentage of Subjects Achieving Greater Than or Equal to (>=) 125 Percent Increase From Baseline in Psoriasis Area and Severity Index (PASI) Scores

End point description:

PASI score is the combined assessment of lesion severity (estimated by 3 components: of erythema, induration and scaling) and area affected into single score range: 0 (no disease) to 72 (maximal disease), with higher scores representing greater severity of psoriasis. Each component of severity, that is, erythema, induration and scaling was assessed separately for four body areas (head and neck [h], upper limbs [u], trunk [t] and lower limbs [l]) on a 5-point scale ranges from 0=no involvement, 1=slight, 2=moderate, 3=marked, 4=very marked. Higher score indicates greater severity. Final PASI score = 0.1Ah (Eh + Ih + Sh) + 0.2Au (Eu + Iu + Su) + 0.3At (Et + It + St) + 0.4Al (El + Il + Sl), where head and neck: 0.1; upper limbs: 0.2; trunk: 0.3; lower limbs: 0.4. Percentage of subjects with >=125% increase from baseline in PASI scores were reported. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2200	566		
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =2194, 555)	0.96 (0.55 to 1.36)	1.08 (0.22 to 1.94)		
Month 3 (n =2200, 566)	1.18 (0.73 to 1.63)	0.71 (0.02 to 1.4)		
Month 6 (n =2048, 557)	1.27 (0.78 to 1.75)	0.9 (0.11 to 1.68)		
Month 12 (n =1775, 525)	0.9 (0.46 to 1.34)	1.33 (0.35 to 2.31)		
Month 24 (n =1393, 445)	0.93 (0.43 to 1.44)	0.9 (0.02 to 1.78)		
Month 36 (n =1118, 380)	0.54 (0.11 to 0.96)	1.32 (0.17 to 2.46)		
Month 48 (n =422, 124)	0.71 (0 to 1.51)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Itch Severity Item (ISI) Scores

End point title	Itch Severity Item (ISI) Scores

End point description:

ISI assessed severity of itching due to psoriasis. ISI was a single item, horizontal numeric rating scale. Subjects were asked to rate their "severity of itching'' due to psoriasis over the past 24 hours on a numeric rating scale anchored by the terms "0=no itching" and "10=worst possible itching" at the ends. Higher scores indicated greater severity of itching. FAS included all subjects who received at least 1 dose of study drug, excluding the subjects who had compliance issues. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and 'n' signifies those subjects who were evaluable at specified time points for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2197	572		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2172, 566)	5.76 (± 2.91)	5.17 (± 3)		
Month 1 (n =2196, 561)	1.88 (± 2.26)	0.92 (± 1.53)		
Month 3 (n =2197, 572)	1.83 (± 2.32)	0.72 (± 1.39)		
Month 6 (n =2047, 560)	1.87 (± 2.33)	0.82 (± 1.51)		
Month 12 (n =1774, 530)	1.79 (± 2.21)	1.08 (± 1.67)		
Month 24 (n =1394, 449)	1.83 (± 2.23)	1.01 (± 1.54)		
Month 36 (n =1117, 383)	1.69 (± 2.12)	1.21 (± 1.72)		
Month 48 (n =417, 127)	1.92 (± 2.3)	1.24 (± 1.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Itch Severity Item (ISI) Scores at Month 1, 3, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Itch Severity Item (ISI) Scores at Month 1, 3, 6, 12, 24, 36 and 48

End point description:

ISI assessed severity of itching due to psoriasis. ISI was a single item, horizontal numeric rating scale. Subjects were asked to rate their "severity of itching'' due to psoriasis over the past 24 hours on a numeric rating scale anchored by the terms "0=no itching" and "10=worst possible itching" at the ends. Higher scores indicated greater severity of itching. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2107	554		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1 (n =2107, 544)	-3.88 (± 3.06)	-4.26 (± 3.07)		
Month 3 (n =2103, 554)	-3.94 (± 3.18)	-4.44 (± 3.06)		
Month 6 (n =1958, 543)	-3.91 (± 3.2)	-4.36 (± 3.14)		
Month 12 (n =1693, 514)	-3.9 (± 3.17)	-4.01 (± 3.3)		
Month 24 (n =1340, 435)	-3.8 (± 3.14)	-4.11 (± 3.17)		
Month 36 (n =1078, 372)	-3.95 (± 3.18)	-3.84 (± 3.06)		
Month 48 (n =411, 126)	-4.03 (± 3.19)	-3.78 (± 3.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI) Scores

End point title	Dermatology Life Quality Index (DLQI) Scores

End point description:

The DLQI is a validated, self-administered, 10-item quality-of-life questionnaire that consists of 10 items that assessed the impact of skin disease on quality of life (daily activities, personal relationships, symptoms and feelings, leisure, work and school, and treatment). Each question was scored on a scale of 0=not at all/not relevant to 3=very much. Response from all of the 10 questions were added to derive the DLQI total scores. Total DLQI scores ranges from 0=not at all to 30=very much, with higher scores indicating greater impairment in quality of life. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2243	582		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2243, 582)	12.73 (± 7.12)	10.95 (± 6.61)		
Month 1 (n =2189, 559)	4.11 (± 5.23)	2.14 (± 3.43)		
Month 6 (n =2028, 557)	3.68 (± 5)	1.67 (± 3.33)		
Month 12 (n =1751, 528)	3.44 (± 4.65)	1.71 (± 2.92)		
Month 24 (n =1361, 441)	3.49 (± 4.71)	1.94 (± 3.29)		
Month 36 (n =1093, 372)	2.97 (± 4.05)	1.98 (± 3.35)		
Month 48 (n =407, 124)	3.2 (± 4.39)	1.81 (± 2.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) Scores at Month 1, 6, 12, 24, 36 and 48

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) Scores at Month 1, 6, 12, 24, 36 and 48

End point description:

The DLQI is a validated, self-administered, 10-item quality-of-life questionnaire that consists of 10 items that assessed the impact of skin disease on quality of life (daily activities, personal relationships, symptoms and feelings, leisure, work and school, and treatment). Each question was scored on a scale of 0=not at all/not relevant to 3=very much. Response from all of the 10 questions were added to derive the DLQI total scores. Total DLQI scores ranges from 0=not at all to 30=very much, with higher scores indicating greater impairment in quality of life. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2163	556		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1 (n =2163, 556)	-8.61 (± 7)	-8.75 (± 6.56)		
Month 6 (n =2005, 554)	-9.14 (± 7.06)	-9.22 (± 6.92)		
Month 12 (n =1730, 525)	-9.23 (± 6.91)	-9.02 (± 6.68)		
Month 24 (n =1345, 438)	-9.08 (± 6.82)	-8.47 (± 6.43)		
Month 36 (n =1083, 369)	-9.47 (± 6.8)	-8.46 (± 6.14)		
Month 48 (n =404, 122)	-8.99 (± 6.74)	-7.78 (± 6.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: 36-Item Short-Form (SF-36) Health Survey Version 2, Acute: Physical Component Summary Scores

End point title	36-Item Short-Form (SF-36) Health Survey Version 2, Acute: Physical Component Summary Scores

End point description:

The SF-36 questionnaire, version 2 is a 36-item generic health status measure. SF-36 evaluates 8 health-related aspects of an individual: physical functioning, role-physical, bodily pain, social functioning, mental health, role emotional, vitality, and general health. The score range for each of the 8 health aspects ranges from 0 (worst) to 100 (best), with higher scores indicating good health condition. Two summary scale scores were computed from the 8 health aspect scores: the Physical Component Summary and the Mental Component Summary. Score range for both summary scale ranges from 0 (worst) to 100 (best), with higher scores indicating good health condition. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2233	580		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2233, 580)	47.31 (± 9.38)	48.94 (± 9.12)		
Month 6 (n =2025, 557)	51.78 (± 8.24)	53.51 (± 7.3)		
Month 12 (n =1750, 524)	51.96 (± 8.13)	53.58 (± 7.19)		
Month 24 (n =1362, 442)	51.91 (± 7.8)	53.15 (± 7.32)		
Month 36 (n =857, 286)	52.01 (± 8.08)	53.05 (± 7.28)		
Month 48 (n =124, 56)	52.93 (± 6.79)	52.36 (± 8.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: 36-Item Short-Form (SF-36) Health Survey Version 2, Acute: Mental Component Summary Scores

End point title	36-Item Short-Form (SF-36) Health Survey Version 2, Acute: Mental Component Summary Scores

End point description:

The SF-36 questionnaire, version 2 is a 36-item generic health status measure. SF-36 evaluates 8 health-related aspects of an individual: physical functioning, role-physical, bodily pain, social functioning, mental health, role emotional, vitality, and general health. The score range for each of the 8 health aspects ranges from 0 (worst) to 100 (best), with higher scores indicating good health condition. Two summary scale scores were computed from the 8 health aspect scores: the Physical Component Summary and the Mental Component Summary. Score range for both summary scale ranges from 0 (worst) to 100 (best), with higher scores indicating good health condition. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2233	580		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2233, 580)	43.51 (± 11.98)	43.96 (± 11.23)		
Month 6 (n =2025, 557)	48.86 (± 10.02)	50.03 (± 9.14)		

Month 12 (n =1750, 524)	49.1 (± 9.89)	49.78 (± 9.28)		
Month 24 (n =1362, 442)	49.22 (± 9.82)	49.66 (± 9.54)		
Month 36 (n =857, 286)	49.21 (± 9.95)	50.17 (± 8.2)		
Month 48 (n =124, 56)	50.14 (± 8.96)	49.6 (± 8.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Patient Global Assessment (PtGA) Response of "Clear" or "Almost Clear"

End point title	Number of Subjects With Patient Global Assessment (PtGA) Response of "Clear" or "Almost Clear"

End point description:

The PtGA evaluated the overall skin disease of subjects at that point in time on a single-item. Subjects provided their response on a 5-point scale ranges from: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe. Higher score indicated greater severity of disease. Subjects who provided their response as "clear (score of 0)" or "almost clear (score of 1)" in PtGA at each specified visit were reported in this endpoint. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2244	583		
Units: subjects				
Baseline: Clear (n =2244, 583)	1	3		
Baseline: Almost Clear (n =2244, 583)	25	16		
Month 1: Clear (n =2192, 561)	211	127		
Month 1: Almost Clear (n =2192, 561)	703	246		
Month 3: Clear (n =2177, 568)	248	174		
Month 3: Almost Clear (n =2177, 568)	762	254		
Month 6: Clear (n =2030, 562)	247	176		
Month 6: Almost Clear (n =2030, 562)	748	265		
Month 12: Clear (n =1758, 530)	209	151		
Month 12: Almost Clear (n =1758, 530)	662	236		
Month 24: Clear (n =1380, 449)	171	111		
Month 24: Almost Clear (n =1380, 449)	502	202		
Month 36: Clear (n =1112, 377)	162	75		
Month 36: Almost Clear (n =1112, 377)	418	183		
Month 48: Clear (n =410, 125)	40	25		
Month 48: Almost Clear (n =410, 125)	151	60		

Statistical analyses

No statistical analyses for this end point

Secondary: Euro Quality of Life- 5-Dimensions (EQ-5D)-Utility Scores

End point title	Euro Quality of Life- 5-Dimensions (EQ-5D)-Utility Scores

End point description:

EQ-5D: subject rated 5-dimension (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression) questionnaire to assess health-related quality of life in terms of a single utility score. Each dimension was assessed on a 3-point scale (1=no problems, 2=some problems, 3=extreme problems, where higher scores=worse health condition). The responses from the 5 dimensions were used to calculate a single utility index value. Scoring formula developed by EuroQol Group assigns a utility value for each dimension in the profile. Score was transformed and results in a total score range -0.594 to 1.000; higher score indicated a better health state. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2242	581		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2242, 581)	0.77 (± 0.19)	0.8 (± 0.17)		
Month 6 (n =2021, 559)	0.87 (± 0.15)	0.91 (± 0.13)		
Month 12 (n =1750, 523)	0.88 (± 0.15)	0.91 (± 0.13)		
Month 24 (n =1364, 443)	0.88 (± 0.14)	0.9 (± 0.14)		
Month 36 (n =857, 284)	0.88 (± 0.14)	0.91 (± 0.12)		
Month 48 (n =124, 56)	0.9 (± 0.13)	0.89 (± 0.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Euro Quality of Life-5-Dimensions (EQ-5D)-Visual Analogue Scale Scores (VAS)

End point title	Euro Quality of Life-5-Dimensions (EQ-5D)-Visual Analogue Scale Scores (VAS)

End point description:

EQ-5D VAS was a subject rated questionnaire to assess health-related quality of life in terms of a single index value. It was a visual analogue scale that ranged from 0 (minimum) to 100 (maximum), with higher scores indicating a better health condition. FAS. Here, 'number of subjects analyzed'= subjects evaluable for this endpoint and n reported.

End point type	Secondary

End point timeframe:

Baseline, Month 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2224	570		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =2224, 570)	66.39 (± 23.2)	68.21 (± 22.91)		
Month 6 (n =2026, 559)	78.28 (± 17.11)	83.95 (± 16.18)		
Month 12 (n =1749, 525)	78.91 (± 16.95)	83.8 (± 14.85)		
Month 24 (n =1365, 443)	79.8 (± 16.98)	83.47 (± 15.55)		
Month 36 (n =856, 286)	79.43 (± 17.01)	84.62 (± 14.28)		
Month 48 (n =124, 56)	82.14 (± 14.07)	84.5 (± 16.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Answered Psoriasis Healthcare Resource Utilization Questionnaire (Ps-HCRU)

End point title	Number of Subjects Who Answered Psoriasis Healthcare Resource Utilization Questionnaire (Ps-HCRU)

End point description:

Ps-HCRU was a short questionnaire designed to assess healthcare resource use and the impact of psoriasis on work. In the first section, it assessed direct costs associated with healthcare resource use which included subject's interactions with healthcare providers such as general practitioners, dermatologists, cardiologists, gastroenterologists, psychiatrists, surgeons and nurses. When taking the evening dose of tofacitinib, subjects were asked to answer the Ps-HCRU questionnaire only if they had an interaction with a healthcare provider or their work was impacted by psoriasis on that specified day. In this endpoint, number of subjects who answered Ps-HCRU at any specified visits were reported.Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 3, 6, 12, 24, 36, 48

End point values	Tofacitinib 10 mg	Tofacitinib 5 mg or 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2281	586		
Units: subjects				
Baseline	156	44		
Month 1	153	30		
Month 3	204	55		

Month 6	288	71		
Month 12	234	71		
Month 24	171	50		
Month 36	114	30		
Month 48	22	11		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 4 weeks after last dose of study drug (up to a maximum of 67 months)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non serious in another subject, or one subject may have experienced both a serious and non serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Tofacitinib 5 mg or 10 mg

Reporting group description:

Subjects received Tofacitinib 10 mg tablets orally twice daily for a period of 3 months. After 3 months of treatment, subjects received twice daily dosing of tofacitinib 5 mg or 10 mg tablets until any safety and efficacy finding requiring study discontinuation (up to a maximum of 66 months). Dose adjustment (5 mg or 10 mg) was assessed on every 3 month visit and was based on investigator's discretion.

Reporting group title	Tofacitinib 10 mg

Reporting group description:

Subjects received Tofacitinib 10 milligram (mg) tablets orally twice daily from Day 1 until any safety finding requiring study discontinuation (up to a maximum of 66 months).

Serious adverse events	Tofacitinib 5 mg or 10 mg	Tofacitinib 10 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 586 (15.02%)	304 / 2281 (13.33%)	
number of deaths (all causes)	7	22	
number of deaths resulting from adverse events	4	9	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acoustic neuroma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	2 / 586 (0.34%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	1 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen’s disease			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 586 (0.00%)	5 / 2281 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	2 / 586 (0.34%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Fibroadenoma of breast			

subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer metastatic			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hairy cell leukaemia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposarcoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma metastatic			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Lung neoplasm			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Malignant melanoma			
subjects affected / exposed	1 / 586 (0.17%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm papilla of Vater			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Metastases to liver			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Metastases to pleura			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal cavity cancer			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oligodendroglioma			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	2 / 2	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	4 / 586 (0.68%)	10 / 2281 (0.44%)	
occurrences causally related to treatment / all	2 / 4	7 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcomatosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine adenocarcinoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	2 / 586 (0.34%)	4 / 2281 (0.18%)	
occurrences causally related to treatment / all	0 / 3	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular malignant teratoma			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Throat cancer			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			

subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subgaleal haematoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vein disorder			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest pain			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Bartholin’s cyst	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic haematoma	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatism	Additional description: This is gender specific event. The number of subjects evaluable for this event are 1641 and 383.		
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp	Additional description: This is gender specific event. The number of subjects evaluable for this event are 640 and 203.		
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
Acute respiratory failure			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bronchitis chronic			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 586 (0.34%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 586 (0.34%)	7 / 2281 (0.31%)	
occurrences causally related to treatment / all	1 / 2	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary thrombosis			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Depression			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device occlusion			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
SEVERE REBOUND PSORIASIS - THE PATIENT’S LAST DOSE OF MEDICATION WAS 06 APR 2015 AND THE PATIENT BEG			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	3 / 586 (0.51%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	3 / 586 (0.51%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			

subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	1 / 586 (0.17%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			

subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 586 (0.00%)	7 / 2281 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Skin abrasion			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haematoma			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 586 (0.34%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	1 / 586 (0.17%)	4 / 2281 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	1 / 3	
Cardiac valve disease			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 586 (0.17%)	5 / 2281 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery occlusion			

subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	2 / 586 (0.34%)	6 / 2281 (0.26%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Myocardial ischaemia			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertonia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic stroke			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 586 (0.34%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Hypoacusis			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tympanic membrane perforation			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	2 / 586 (0.34%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	2 / 586 (0.34%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital fat herniation			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn’s disease			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Noninfective sialoadenitis			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 586 (0.17%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertensive gastropathy			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland disorder			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythrodermic psoriasis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 586 (0.17%)	6 / 2281 (0.26%)	
occurrences causally related to treatment / all	1 / 1	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pustular psoriasis			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	2 / 586 (0.34%)	4 / 2281 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular acidosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic nodular goitre			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
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			
Arthralgia			
subjects affected / exposed	2 / 586 (0.34%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 586 (0.34%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 586 (0.34%)	5 / 2281 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament disorder			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			

subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 586 (0.00%)	7 / 2281 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacroiliitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal disorder			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal instability			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 586 (0.34%)	5 / 2281 (0.22%)	
occurrences causally related to treatment / all	1 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteriuria			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartonellosis			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 586 (0.00%)	3 / 2281 (0.13%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 586 (0.00%)	6 / 2281 (0.26%)	
occurrences causally related to treatment / all	0 / 0	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis staphylococcal			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 586 (0.17%)	6 / 2281 (0.26%)	
occurrences causally related to treatment / all	1 / 1	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			

subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer helicobacter			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex meningitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 586 (0.00%)	7 / 2281 (0.31%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Listeria encephalitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis bacterial			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 586 (0.85%)	16 / 2281 (0.70%)	
occurrences causally related to treatment / all	2 / 5	11 / 16	
deaths causally related to treatment / all	0 / 0	3 / 3	
Pneumonia influenzal			
subjects affected / exposed	2 / 586 (0.34%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 586 (0.17%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulence			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			

subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 586 (0.17%)	4 / 2281 (0.18%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 586 (0.34%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 586 (0.00%)	4 / 2281 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 586 (0.17%)	0 / 2281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 586 (0.00%)	1 / 2281 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 586 (0.00%)	2 / 2281 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tofacitinib 5 mg or 10 mg	Tofacitinib 10 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	394 / 586 (67.24%)	1415 / 2281 (62.03%)	
Investigations			
Blood cholesterol increased			
subjects affected / exposed	33 / 586 (5.63%)	86 / 2281 (3.77%)	
occurrences (all)	38	104	
Blood creatine phosphokinase			

increased			
subjects affected / exposed	92 / 586 (15.70%)	294 / 2281 (12.89%)	
occurrences (all)	118	392	
Gamma-glutamyltransferase increased			
subjects affected / exposed	38 / 586 (6.48%)	81 / 2281 (3.55%)	
occurrences (all)	48	96	
Vascular disorders			
Hypertension			
subjects affected / exposed	44 / 586 (7.51%)	169 / 2281 (7.41%)	
occurrences (all)	48	180	
Nervous system disorders			
Headache			
subjects affected / exposed	38 / 586 (6.48%)	119 / 2281 (5.22%)	
occurrences (all)	49	177	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	32 / 586 (5.46%)	73 / 2281 (3.20%)	
occurrences (all)	35	80	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	39 / 586 (6.66%)	148 / 2281 (6.49%)	
occurrences (all)	45	172	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	40 / 586 (6.83%)	164 / 2281 (7.19%)	
occurrences (all)	44	191	
Infections and infestations			
Bronchitis			
subjects affected / exposed	48 / 586 (8.19%)	134 / 2281 (5.87%)	
occurrences (all)	61	166	
Herpes zoster			
subjects affected / exposed	33 / 586 (5.63%)	136 / 2281 (5.96%)	
occurrences (all)	34	141	
Influenza			
subjects affected / exposed	23 / 586 (3.92%)	126 / 2281 (5.52%)	
occurrences (all)	30	163	
Nasopharyngitis			

subjects affected / exposed	122 / 586 (20.82%)	476 / 2281 (20.87%)	
occurrences (all)	208	878	
Upper respiratory tract infection			
subjects affected / exposed	51 / 586 (8.70%)	264 / 2281 (11.57%)	
occurrences (all)	84	428	
Urinary tract infection			
subjects affected / exposed	42 / 586 (7.17%)	145 / 2281 (6.36%)	
occurrences (all)	69	209	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	52 / 586 (8.87%)	73 / 2281 (3.20%)	
occurrences (all)	66	88	
Hypercholesterolaemia			
subjects affected / exposed	30 / 586 (5.12%)	134 / 2281 (5.87%)	
occurrences (all)	35	159	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2011	1. Proposed INN changed from tasocitinib to tofacitinib since WHO did not accept the name tasocitinib; 2. Protocol Summary, Study Design updated to clarify that beyond Month 12, study visit frequency occurs every three months up to at least two years post First Market Approval in a global, major market; 3. Section 7.1: Modified requirements for the psoriasis evaluator 1) to be a dermatologist (board certified or equivalent); an experienced and qualified non-dermatologist physician or medical professional may be permitted to perform these evaluations with approval of the Pfizer Clinician or designee, and 2) the same evaluator for a given subject to begin at the Baseline/Day 1 visit instead of the Screening visit(s) because the Screening psoriasis assessments are not used in data analysis.
25 October 2012	1.Protocol language updated globally to match CT02 language revisions: All references to "legally acceptable representative" changed to "legal representative" throughout document; Section 4.4.7.1 - changed "adequate" to "highly effective" method of contraception, clarified "one ovulatory cycle" by replacing with "at least 28 days", added "correctly placed" and "or Intrauterine system (IUS)" to Intrauterine device method of contraception; 2. Exclusion criteria 4.2.2 added: Absolute lymphocyte count of <0.5 x 10^9 /L (<500/mm^3) at screening visit; 3.Section 9.5 Data Monitoring Committee name was changed to Data Safety Monitoring Board; 4. Study A3921147 has been added to the list of qualifying studies throughout the document; 5.Appendix 1: Additional medication armodafinil (Nuvigil) added to Prohibited Concomitant Medications list of moderate CYP3A inducers.Study Investigators were notified of this change by letter on 25 JAN 2012, and were notified that this change would be added to the protocol when an amendment was needed.
08 April 2013	1. Additional Hepatitis B test information added; 2. Single positive HBc Ab and a negative HBs Ab was added as a reason for subject discontinuation; 3.Name Tofacitinib citrate added.
01 May 2015	1.Sponsor designation of "CP-690,550" replaced by generic name "tofacitinib" throughout document except on title page and at initial appearance of "CP-690,550" in Section 1.1; 2. Section 4.4.5: removed ECG; 3. Sections 5.3.3 and 5.3.4: deleted dosing diary and compliance text based on dosing diary. Updated text for medication errors; 4. Section 6:deleted reference to ECG throughout section; 5. Section 6.2: deleted dosing diary reference, Short form 36 questionnaire (SF-36), EuroQoL 5 Dimensions (EQ 5D), Psoriasis Health Care Resource Utilization (Ps-HCRU); updated language regarding adjudication review; 6. Section 6.4.1: deleted PROs, vital signs, weight, waist and hip circumference, targeted physical exam, lipid panel, urinalysis, PASI, PGA, BSA, dosing diary; 7. Section 7.2: deleted SF-36, EQ 5D, Ps-HCRU; 8. Section 7.2.2 SF-36: deleted section; 9. Section 7.2.4 Ps-HCRU: deleted section; 10.Section 7.2.3 EC-5D: deleted section; 11. In Appendix 10: A3921061 Immunogenicity Substudy, pneumococcal data updated to titers/concentrations; Ig G "concentrations" rather than "titers" were evaluated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

08 March 2016	The study was terminated by the sponsor on 08 March 2016 as it had met its objectives of characterizing long-term safety and tolerability.The study termination was not due to any safety concerns	-

Notes:

Limitations and caveats

None reported