Clinical trial results:
A Long-term, Open-Label Extension Study of Tofacitinib (CP-690,550) for the Treatment of Psoriatic Arthritis

Summary

EudraCT number	2011-002169-39
Trial protocol	BE HU CZ BG SK PL ES DE
Global end of trial date	20 May 2019

Results information

Result version number	v1 (current)
This version publication date	22 May 2020
First version publication date	22 May 2020

Trial information

Trial identification

Sponsor protocol code	A3921092

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 May 2019
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 (5 mg twice daily [BID] and 10 mg BID) in adult subjects with active Psoriatic Arthritis (PsA) and to evaluate the long term efficacy of treatment with tofacitinib (5 mg BID and 10 mg BID) in adult subjects with active Psoriatic Arthritis (PsA)

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2014
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	Belgium: 17
Country: Number of subjects enrolled	Brazil: 7
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czech Republic: 18
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	Mexico: 56
Country: Number of subjects enrolled	Poland: 196
Country: Number of subjects enrolled	Russian Federation: 63
Country: Number of subjects enrolled	Slovakia: 12
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Taiwan: 13
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	United States: 133
Country: Number of subjects enrolled	Australia: 22
Worldwide total number of subjects	686
EEA total number of subjects	390

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)	625
From 65 to 84 years	61
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible subjects (who had previously participated in randomized PsA clinical studies with tofacitinib) from qualifying studies A3921091 (NCT01877668) and A3921125 (NCT01882439) were enrolled into this current study A3921092 (NCT01976364).

Pre-assignment

Screening details:

This main study was a long-term extension study, which also included a sub-study only for the purpose of efficacy, safety and tolerability of tofacitinib monotherapy as compared to tofacitinib combination therapy with methotrexate. Sub-study included eligible subjects from main study who consented to take part in sub-study.

Period 1

Period 1 title	Main Study (36 Months)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Tofacitinib

Arm description:

Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib 5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tofacitinib 5 mg oral tablet, BID for 36 months.

Investigational medicinal product name	Tofacitinib 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets of Tofacitinib 5 mg orally, BID for 36 months.

Number of subjects in period 1	Tofacitinib
Started	686
Completed	465
Not completed	221
Adverse event, serious fatal	5
Consent withdrawn by subject	69

Adverse event, non-fatal	63
Withdrawn due to pregnancy	5
No longer met eligibility criteria	2
Medication error	1
Unspecified	13
Lost to follow-up	10
Lack of efficacy	40
Protocol deviation	13

Period 2

Period 2 title	Sub-study (12 Months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib 5 mg BID + Methotrexate (MTX)

Arm description:

Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib 5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tofacitinib 5 mg oral tablet BID for up to 12 months.

Investigational medicinal product name	Methotrexate (MTX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

MTX capsules orally (dose range from 7.5 mg to 20 mg per week), for up to 12 months.

Arm title	Tofacitinib 5 mg BID + Placebo

Arm description:

Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months.

Arm type	Experimental

Investigational medicinal product name	Tofacitinib 5 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tofacitinib 5 mg oral tablet BID for up to 12 months.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

MTX matched placebo capsules orally weekly for up to 12 months.

Number of subjects in period 2[1]	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo
Started	89	90
Completed	83	85
Not completed	6	5
Consent withdrawn by subject	-	1
Adverse event, non-fatal	4	3
Lost to follow-up	1	-
Protocol deviation	1	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects from main study who consented to take part in sub-study, continued into sub-study.

Baseline characteristics

Reporting groups	
Reporting group title	Main Study (36 Months)

Reporting group description: -

Reporting group values	Main Study (36 Months)	Total	
Number of subjects	686	686	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	625	625	
From 65-84 years	61	61	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	48.8		
standard deviation	± 11.8	-	
Sex: Female, Male Units: Subjects			
Female	370	370	
Male	316	316	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	21	21	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	2	
White	646	646	
More than one race	17	17	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Tofacitinib

Reporting group description:

Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion.

Reporting group title	Tofacitinib 5 mg BID + Methotrexate (MTX)

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months.

Reporting group title	Tofacitinib 5 mg BID + Placebo

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months.

Subject analysis set title	All Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Main Study: Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion. Sub-study: Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX capsules orally (dose range from 7.5 to 20 mg per week) or tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules, for up to 12 months.

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

End point title	Percentage 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. 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 48 months that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non -serious AEs. SAS included all subjects enrolled in this study who were part of a prior qualifying study, and who received at least one dose of open-label study medication in A3921092. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol.

End point type	Primary

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 analyzed for this endpoint.

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	686			
Units: percentage of subjects				
number (not applicable)				
AEs	83.7			
SAEs	16.8			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Adverse Events (AEs) by Severity

End point title	Number of Adverse Events (AEs) 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 into 3 categories according to their severity as mild AEs (did not interfere with subject's usual function), moderate AEs (interfered to some extent with subject's usual function) and severe AEs (interfered significantly with subject's usual function). SAS included all subjects enrolled in this study who were part of a prior qualifying study, and who received at least one dose of open-label study medication in A3921092. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol.

End point type	Primary

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 analyzed for this endpoint.

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	686			
Units: adverse events				
Number of adverse events: Mild	1632			
Number of adverse events: Moderate	1045			
Number of adverse events: Severe	136			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Clinical Laboratory Values

End point title	Number of Subjects With Abnormal Clinical Laboratory Values[3]

End point description:

Laboratory tests: hematology (Hb, hematocrit, RBC count, platelets, reticulocytes, WBC count, count and absolute lymphocytes,neutrophils, basophils, eosinophils, monocytes. Liver function (bilirubin [total, direct, indirect], AST, ALT, alkaline phosphatase, gamma-glutamyl transferase, albumin, total protein),

renal function (blood urea nitrogen, creatinine), Lipids (cholesterol, HDL, LDL, triglyceride, apolipoprotein [A-1, B]), electrolytes (sodium, potassium, chloride, calcium, biocarbonate), chemistry (glucose, HbA1c, creatinine kinapse), urinalysis dipstick(urine pH, glucose, ketones, protein, blood, leukocyte, esterase), urinalysis microscopy (urine- RBC, WBC, bacteria, epithelial cells),C-reactive protein. Laboratory abnormality: determined by investigator per pre-defined criteria. SAS was analyzed. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol. Number of Subjects Analyzed= Subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 analyzed for this endpoint.

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	683			
Units: subjects				
number (not applicable)	646			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change from Baseline in Clinical Laboratory Values

End point title	Number of Subjects With Clinically Significant Change from Baseline in Clinical Laboratory Values[4]

End point description:

Laboratory tests: hematology (Hb, hematocrit, RBC count, platelets, reticulocytes, WBC count, count and absolute lymphocytes, neutrophils, basophils, eosinophils, monocytes. Liver function (bilirubin[total,direct,indirect], AST, ALT, alkaline phosphatase, gamma-glutamyl transferase, albumin, total protein), renal function (blood urea nitrogen, creatinine), Lipids(cholesterol, HDL, LDL, triglyceride, apolipoprotein [A-1, B]), electrolytes (sodium, potassium, chloride, calcium, biocarbonate), chemistry (glucose, HbA1c, creatinine kinapse), urinalysis dipstick(urine-pH, glucose, ketones, protein, blood, leukocyte, esterase), urinalysis microscopy(urine- RBC, WBC, bacteria, epithelial cells),C-reactive protein. Clinically significant change: determined by investigator per pre-defined criteria. SAS was analyzed. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol.

End point type	Primary

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 analyzed for this endpoint.

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	686			
Units: Subjects				
number (not applicable)	9			

Statistical analyses

No statistical analyses for this end point

Primary: Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 6

End point title	Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 6

End point description:

HAQ-DI assessed the degree of difficulty a subject had experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in each of these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible HAQ-DI score ranged from 0 (least difficulty) to 3 (extreme difficulty), where higher score indicated more difficulty while performing daily living activities. Full analysis set (FAS) of sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Primary

End point timeframe:

Sub-study: Baseline (Day 1), Month 6

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)	0.0174 (± 0.02775)	0.0428 (± 0.02714)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Analysis was based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least Square (LS) Mean difference
Point estimate	0.0255
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0513
upper limit	0.1022

Primary: Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Month 6

End point title	Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Month 6

End point description:

PASDAS was composite PsA disease activity score that included following components:Physician and patient global assessment of disease activity (assessed on a 0-100 VAS) in millimeter (mm), swollen (66 joints) and tender joint counts (68 joints), Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6), tender dactylitic digit score (scored on a scale of 0-3, where 0= no tenderness and 3= extreme tenderness), short form-36 questionnaire (SF-36) physical component summary (norm-based domain scores were used in analyses; with a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity) and C-reactive protein (CRP) in milligram per liter (mg/L). PASDAS was composite score and was a weighted index with score range of 0 to 10, where higher score indicated more severe disease. FAS of main study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Primary

End point timeframe:

Sub-study: Baseline (Day 1), Month 6

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)	0.138 (± 0.0805)	0.229 (± 0.0786)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Results are based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.091
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.131
upper limit	0.313

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 20 Percent (%) (ACR20) Response

End point title	Main Study: Percentage of Subjects Achieving an American College of Rheumatology 20 Percent (%) (ACR20) Response

End point description:

Subjects with 20% improvement from baseline in tender and swollen joint counts and 20% improvement in at least 3 of the 5 measures: Patient’s global assessment of arthritis (PtGA), Physician’s global assessment of arthritis (PhyGA), subject's assessment of arthritis pain, HAQ-DI and C-reactive protein (CRP) in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0(no pain) to 100 mm(extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm(no pain) to 100 mm(most severe pain), higher score=more pain. HAQ-DI: functional disability evaluation, score: 0(no difficulty) to 3(extreme difficulty),higher score implied more disability. FAS population for long-term extension (LTE) main study. n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n = 673)	66.12 (62.55 to 69.70)			
Month 3 (n =660)	68.79 (65.25 to 72.32)			
Month 6 (n =634)	70.66 (67.12 to 74.21)			
Month 9 (n =603)	71.48 (67.87 to 75.08)			
Month 12 (n =581)	74.18 (70.62 to 77.74)			
Month 15 (n =551)	78.04 (74.58 to 81.50)			
Month 18 (n =537)	77.65 (74.13 to 81.18)			
Month 21 (n =526)	77.00 (73.40 to 80.59)			

Month 24 (n =511)	76.13 (72.43 to 79.82)			
Month 27 (n =495)	78.18 (74.54 to 81.82)			
Month 30 (n =479)	80.79 (77.27 to 84.32)			
Month 33 (n =452)	77.88 (74.05 to 81.70)			
Month 36 (n =383)	77.02 (72.81 to 81.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 50% (ACR50) Response

End point title	Main Study: Percentage of Subjects Achieving an American College of Rheumatology 50% (ACR50) Response

End point description:

Subjects with 50% improvement from baseline in tender and swollen joint counts and 50% improvement in at least 3 of the 5 measures: PtGA, PhyGA, subject's assessment of arthritis pain, HAQ-DI and CRP in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm (no pain) to 100 mm (most severe pain), higher score =more pain. HAQ-DI: functional disability evaluation, score: 0 (no difficulty) to 3 (extreme difficulty), higher score implied more disability. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =674)	45.70 (41.94 to 49.46)			
Month 3 (n =661)	43.27 (39.49 to 47.04)			
Month 6 (n =633)	47.08 (43.19 to 50.97)			
Month 9 (n =605)	50.41 (46.43 to 54.40)			
Month 12 (n =581)	50.26 (46.19 to 54.32)			
Month 15 (n =554)	55.42 (51.28 to 59.55)			
Month 18 (n =539)	55.10 (50.90 to 59.30)			

Month 21 (n =527)	55.41 (51.16 to 59.65)			
Month 24 (n =511)	57.34 (53.05 to 61.63)			
Month 27 (n =496)	56.05 (51.68 to 60.42)			
Month 30 (n =478)	60.46 (56.08 to 64.84)			
Month 33 (n =452)	57.96 (53.41 to 62.52)			
Month 36 (n =384)	58.85 (53.93 to 63.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 70% (ACR70) Response

End point title	Main Study: Percentage of Subjects Achieving an American College of Rheumatology 70% (ACR70) Response

End point description:

Subjects with 70% improvement from baseline in tender and swollen joint counts and 70% improvement in at least 3 of the 5 measures: PtGA, PhyGA, subject's assessment of arthritis pain, HAQ-DI and CRP in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm (no pain) to 100 mm (most severe pain), higher score =more pain. HAQ-DI: functional disability evaluation, score: 0 (no difficulty) to 3 (extreme difficulty), higher score implied more disability. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: percentage of participants				
number (confidence interval 95%)				
Month 1 (n =676)	24.85 (21.59 to 28.11)			
Month 3 (n =662)	26.13 (22.79 to 29.48)			
Month 6 (n =636)	30.50 (26.92 to 34.08)			
Month 9 (n =607)	30.81 (27.13 to 34.48)			
Month 12 (n =582)	32.13 (28.34 to 35.92)			
Month 15 (n =555)	33.87 (29.94 to 37.81)			

Month 18 (n =538)	36.25 (32.18 to 40.31)			
Month 21 (n =527)	34.35 (30.29 to 38.40)			
Month 24 (n =512)	35.94 (31.78 to 40.09)			
Month 27 (n =496)	38.10 (33.83 to 42.38)			
Month 30 (n =476)	41.60 (37.17 to 46.02)			
Month 33 (n =453)	38.19 (33.72 to 42.66)			
Month 36 (n =384)	37.76 (32.91 to 42.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

HAQ-DI assessed the degree of difficulty a participant had experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain score and divided by the number of domains answered. Total possible score range 0 (least difficulty) and 3 (extreme difficulty), where higher score indicate more difficulty while performing daily living activities. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =675)	-0.4373 (± 0.55677)			
Change at Month 3 (n =661)	-0.4559 (± 0.55104)			
Change at Month 6 (n =636)	-0.4755 (± 0.57468)			
Change at Month 9 (n =605)	-0.4841 (± 0.58294)			
Change at Month 12 (n =582)	-0.4782 (± 0.60163)			

Change at Month 15 (n =554)	-0.5108 (± 0.58277)			
Change at Month 18 (n =539)	-0.5116 (± 0.59401)			
Change at Month 21 (n =528)	-0.5211 (± 0.59568)			
Change at Month 24 (n =511)	-0.5068 (± 0.62016)			
Change at Month 27 (n =496)	-0.5219 (± 0.60833)			
Change at Month 30 (n =478)	-0.5356 (± 0.61316)			
Change at Month 33 (n =453)	-0.5276 (± 0.63803)			
Change at Month 36 (n =386)	-0.5476 (± 0.65226)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC)

End point title	Main Study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC)

End point description:

PsARC was comprised of 4 clinical improvement criteria: greater than or equal to (>=) 20% improvement in PhyGA (VAS), >=20% improvement in patient's global assessment of arthritis (PtGA); and >=30% reduction in the number of tender joints; and >=30% reduction in the number of swollen joints. PtGA: subject assessed health on VAS, 0 mm (very well) to 100 mm (worst health condition), higher score = worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. To achieve a clinical response, the subject must improve in 2 of the 4 PsARC criteria, 1 of which has to be the number of tender or swollen joints and none of the 4 score could worsen. FAS population for LTE main study was analyzed. "n"= subjects evaluable for this outcome measure at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =669)	68.46 (64.94 to 71.98)			
Month 3 (n =657)	69.56 (66.04 to 73.08)			
Month 6 (n =633)	73.14 (69.69 to 76.60)			
Month 9 (n =599)	74.46 (70.97 to 77.95)			

Month 12 (n =577)	76.08 (72.60 to 79.56)			
Month 15 (n =547)	79.52 (76.14 to 82.91)			
Month 18 (n =534)	80.15 (76.77 to 83.53)			
Month 21 (n =522)	79.50 (76.04 to 82.96)			
Month 24 (n =507)	77.51 (73.88 to 81.15)			
Month 27 (n =494)	80.16 (76.65 to 83.68)			
Month 30 (n =475)	82.11 (78.66 to 85.55)			
Month 33 (n =449)	80.85 (77.21 to 84.49)			
Month 36 (n =381)	77.17 (72.95 to 81.38)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects with Baseline PGA-PsO Score Greater Than [>]0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects with Baseline PGA-PsO Score Greater Than [>]0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

The PGA-PsO was a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling were scored separately over the whole body according to a 5-point severity scale (0-4). Higher score indicated higher disease severity. Severity score for each erythema, induration and scaling were summed and averaged after which the total average was rounded to the nearest whole number score to determine a PGA-PsO score on a scale of 0 to 4 (0= clear, except for any residual discoloration, 1= almost clear, 2= mild, 3= moderate, 4= severe). Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline PGA-PsO score >0. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	660			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =649)	-1.1 (± 1.04)			
Change at Month 3 (n =636)	-1.1 (± 1.04)			
Change at Month 6 (n =610)	-1.2 (± 1.03)			

Change at Month 9 (n =578)	-1.2 (± 1.06)			
Change at Month 12 (n =559)	-1.1 (± 1.06)			
Change at Month 15 (n =532)	-1.2 (± 1.07)			
Change at Month 18 (n =516)	-1.2 (± 1.05)			
Change at Month 21 (n =506)	-1.2 (± 1.06)			
Change at Month 24 (n =488)	-1.3 (± 1.02)			
Change at Month 27 (n =478)	-1.3 (± 1.02)			
Change at Month 30 (n =462)	-1.3 (± 1.05)			
Change at Month 33 (n =434)	-1.3 (± 1.02)			
Change at Month 36 (n =372)	-1.2 (± 1.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects With a Psoriasis Area and Severity Index 75 (PASI75) Score (For Subjects With Baseline Body Surface Area [BSA]>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Percentage of Subjects With a Psoriasis Area and Severity Index 75 (PASI75) Score (For Subjects With Baseline Body Surface Area [BSA]>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

PASI:combined assessment of lesion severity and body area affected into single score;range=0(no disease)-72(maximal disease).Higher score represented greater severity of psoriasis. PASI was composite scoring by investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated:0(0%) - 6(90-100%) and severity estimated by clinical signs of erythema, induration, scaling; ranged 0 4: 0=none,1=slight,2=moderate,3=marked,4=very marked.Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1,upper limbs=0.2,trunk=0.3,lower limbs=0.4). PASI75: >= 75% reduction in PASI relative to Baseline. FAS of main study with baseline: BSA>=3%, PASI score > 0. n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	474			
Units: percentage of subjects				
number (confidence interval 95%)				
Month 1 (n =465)	55.05 (50.53 to 59.58)			
Month 3 (n =452)	57.96 (53.41 to 62.52)			
Month 6 (n =433)	60.74 (56.14 to 65.34)			
Month 9 (n =411)	61.07 (56.36 to 65.78)			

Month 12 (n =399)	63.16 (58.42 to 67.89)			
Month 15 (n =382)	65.71 (60.95 to 70.47)			
Month 18 (n =368)	65.22 (60.35 to 70.08)			
Month 21 (n =360)	69.72 (64.98 to 74.47)			
Month 24 (n =347)	71.47 (66.72 to 76.22)			
Month 27 (n =343)	70.85 (66.04 to 75.66)			
Month 30 (n =331)	68.58 (63.58 to 73.58)			
Month 33 (n =311)	70.10 (65.01 to 75.18)			
Month 36 (n =260)	68.08 (62.41 to 73.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percent Change From Baseline in PASI Composite Score (For Subjects With Baseline BSA>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Percent Change From Baseline in PASI Composite Score (For Subjects With Baseline BSA>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

PASI: combined assessment of lesion severity & area affected into single score; range=0(no disease)-72(maximal disease). Higher score represented greater severity of psoriasis. PASI is a composite scoring by investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated: 0(0%) - 6(90-100%) & severity estimated by clinical signs of erythema, induration, scaling; ranged 0-4: 0=none, 1=slight, 2=moderate, 3=marked, 4=very marked. Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4). FAS of main study with baseline: BSA>=3%, PASI score >0. n =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main study: Baseline, Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	474			
Units: percent change				
arithmetic mean (standard deviation)				
At Month 1 (n =465)	-64.09 (± 57.473)			

At Month 3 (n =452)	-66.98 (± 43.647)			
At Month 6 (n =433)	-68.58 (± 44.568)			
At Month 9 (n =411)	-70.42 (± 40.617)			
At Month 12 (n =399)	-71.58 (± 42.515)			
At Month 15 (n =382	-73.13 (± 43.653)			
At Month 18 (n =368)	-73.51 (± 40.527)			
At Month 21 (n =360)	-75.15 (± 44.182)			
At Month 24 (n =347)	-78.36 (± 34.808)			
At Month 27 (n =343)	-78.37 (± 34.405)			
At Month 30 (n =331)	-78.28 (± 30.270)			
At Month 33 (n =311)	-77.47 (± 43.952)			
At Month 36 (n =260)	-76.85 (± 31.973)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percent Change From Baseline in PASI Clinical Signs Component Score (For Subjects With Baseline BSA>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Percent Change From Baseline in PASI Clinical Signs Component Score (For Subjects With Baseline BSA>=3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

PASI: combined assessment of lesion severity & area affected into single score; range=0(no disease)-72(maximal disease). Higher score representing greater severity of psoriasis. PASI was a composite scoring by investigator of degree of clinical sign components for erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated: 0(0%) - 6(90-100%) and severity estimated by clinical signs components for erythema, induration, scaling; ranged 0-4: 0=none, 1=slight, 2=moderate, 3=marked, 4=very marked. Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4). Analysis population included FAS of main study with baseline BSA>=3%, baseline PASI score >0. n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main study: Baseline(Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	474			
Units: percent change				
arithmetic mean (standard deviation)				
Induration: At Month 1 (n =456)	-62.60 (± 62.288)			
Induration: At Month 3 (n =442)	-66.92 (± 46.898)			
Induration: At Month 6 (n =423)	-68.63 (± 46.644)			
Induration: At Month 9 (n =402)	-70.33 (± 41.960)			
Induration: At Month 12 (n =390)	-70.81 (± 48.439)			
Induration: At Month 15 (n =373)	-72.49 (± 48.644)			
Induration: At Month 18 (n =359)	-73.16 (± 40.801)			
Induration: At Month 21 (n =352)	-74.34 (± 47.617)			
Induration: At Month 24 (n =338)	-78.45 (± 36.534)			
Induration: At Month 27 (n =335)	-77.85 (± 34.297)			
Induration: At Month 30 (n =322)	-78.55 (± 31.187)			
Induration: At Month 33 (n =303)	-77.09 (± 42.305)			
Induration: At Month 36 (n =256)	-76.11 (± 35.000)			
Erythema: At Month 1 (n =464)	-63.60 (± 67.818)			
Erythema: At Month 3 (n =451)	-66.69 (± 43.013)			
Erythema: At Month 6 (n =432)	-67.17 (± 46.756)			
Erythema: At Month 9 (n =410)	-69.75 (± 42.882)			
Erythema: At Month 12 (n =398)	-70.45 (± 46.575)			
Erythema: At Month 15 (n =381)	-71.55 (± 50.406)			
Erythema: At Month 18 (n =367)	-73.12 (± 45.194)			
Erythema: At Month 21 (n =359)	-75.06 (± 45.993)			
Erythema: At Month 24 (n =346)	-77.40 (± 38.093)			
Erythema: At Month 27 (n =342)	-77.83 (± 33.877)			
Erythema: At Month 30 (n =330)	-77.04 (± 33.478)			
Erythema: At Month 33 (n =310)	-75.17 (± 53.782)			
Erythema: At Month 36 (n =259)	-75.72 (± 34.823)			
Scaling: At Month 1 (n =453)	-64.26 (± 55.848)			
Scaling: At Month 3 (n =439)	-66.15 (± 52.568)			

Scaling: At Month 6 (n =420)	-68.66 (± 49.145)			
Scaling: At Month 9 (n =399)	-69.09 (± 48.506)			
Scaling: At Month 12 (n =387)	-72.48 (± 45.755)			
Scaling: At Month 15 (n =370)	-73.83 (± 42.528)			
Scaling: At Month 18 (n =356)	-74.62 (± 39.708)			
Scaling: At Month 21 (n =348)	-75.11 (± 44.570)			
Scaling: At Month 24 (n =336)	-77.86 (± 38.041)			
Scaling: At Month 27 (n =332)	-79.34 (± 31.825)			
Scaling: At Month 30 (n =322)	-77.23 (± 37.819)			
Scaling: At Month 33 (n =302)	-77.94 (± 41.688)			
Scaling: At Month 36 (n =253)	-78.10 (± 30.391)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects With Baseline DSS greater than [>] 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects With Baseline DSS greater than [>] 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis severity score for a participant was 0-60. Higher score indicated greater severity.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	366			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =360)	-6.7 (± 7.65)			
Change at Month 3 (n =352)	-6.8 (± 7.71)			
Change at Month 6 (n =335)	-7.2 (± 7.89)			
Change at Month 9 (n =313)	-7.4 (± 7.29)			

Change at Month 12 (n =305)	-7.6 (± 7.70)			
Change at Month 15 (n =290)	-7.7 (± 7.44)			
Change at Month 18 (n =282)	-7.7 (± 7.50)			
Change at Month 21 (n =275)	-7.8 (± 7.89)			
Change at Month 24 (n =269)	-7.9 (± 7.76)			
Change at Month 27 (n =265)	-8.1 (± 7.59)			
Change at Month 30 (n =257)	-8.0 (± 7.65)			
Change at Month 33 (n =250)	-8.1 (± 7.75)			
Change at Month 36 (n =212)	-7.7 (± 7.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects With Baseline LEI >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects With Baseline LEI >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline LEI >0. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	458			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =449)	-1.5 (± 1.88)			
Change at Month 3 (n =437)	-1.6 (± 1.79)			
Change at Month 6 (n =418)	-1.7 (± 1.78)			
Change at Month 9 (n =398)	-1.8 (± 1.80)			
Change at Month 12 (n =380)	-1.7 (± 1.82)			
Change at Month 15 (n =364)	-2.0 (± 1.76)			
Change at Month 18 (n =347)	-1.9 (± 1.79)			
Change at Month 21 (n =340)	-1.9 (± 1.81)			
Change at Month 24 (n =327)	-2.0 (± 1.72)			
Change at Month 27 (n =317)	-2.0 (± 1.73)			
Change at Month 30 (n =306)	-2.0 (± 1.76)			
Change at Month 33 (n =288)	-2.0 (± 1.75)			

Change at Month 36 (n =253)	-2.1 (± 1.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index (For Subjects with baseline SPARCC Enthesitis Index >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index (For Subjects with baseline SPARCC Enthesitis Index >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

The SPARCC enthesitis index identifies the presence or absence of tenderness at 16 enthesial sites, including (right and left): medial epicondyle humerus, lateral epicondyle humerus, supraspinatus insertion into greater tuberosity of humerus, greater trochanter, quadriceps insertion into superior border of patella, patellar ligament insertion into inferior pole of patella or tibial tubercle, Achilles tendon insertion into calcaneum and plantar fascia insertion into calcaneum. On examination, tenderness is recorded as present (1) or absent (0) for each of the 16 sites, with an overall total score ranging from 0 to 16. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline SPARCC enthesitis index >0. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	525			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =517)	-2.8 (± 3.60)			
Change at Month 3 (n =504)	-3.0 (± 3.61)			
Change at Month 6 (n =481)	-3.2 (± 3.72)			
Change at Month 9 (n =457)	-3.4 (± 3.69)			
Change at Month 12 (n =438)	-3.5 (± 3.46)			
Change at Month 15 (n =415)	-3.7 (± 3.55)			
Change at Month 18 (n =400)	-3.5 (± 3.45)			
Change at Month 21 (n =394)	-3.6 (± 3.60)			
Change at Month 24 (n =379)	-3.7 (± 3.62)			
Change at Month 27 (n =369)	-3.7 (± 3.56)			
Change at Month 30 (n =359)	-3.8 (± 3.49)			
Change at Month 33 (n =340)	-3.9 (± 3.39)			
Change at Month 36 (n =290)	-3.9 (± 3.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects with Presence of Spondylitis at Screening and Baseline BASDAI Score >0 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects with Presence of Spondylitis at Screening and Baseline BASDAI Score >0 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

BASDAI was a validated self-assessment tool used to determine disease activity in subjects with ankylosing spondylitis. Utilizing a VAS of 0-10 cm (0= none and 10= very severe) subjects answered 6 questions pertaining to 5 symptoms including fatigue, spinal pain, joint pain/swelling, areas of localized tenderness and morning stiffness. The final BASDAI score was an average of answers to 6 questions, with an overall possible score range of 0 to 10 centimeter (cm) with higher score represented more severe ankylosing spondylitis disease activity. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 with presence of spondylitis at screening and baseline BASDAI Score >0 cm. n =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	124			
Units: centimeter				
arithmetic mean (standard deviation)				
Change at Month 1 (n =124)	-2.26 (± 2.367)			
Change at Month 3 (n =121)	-2.10 (± 2.278)			
Change at Month 6 (n =116)	-2.40 (± 2.371)			
Change at Month 9 (n =106)	-2.35 (± 2.254)			
Change at Month 12 (n =105)	-2.41 (± 2.371)			
Change at Month 15 (n =99)	-2.35 (± 2.547)			
Change at Month 18 (n =95)	-2.41 (± 2.640)			
Change at Month 21 (n =89)	-2.28 (± 2.582)			

Change at Month 24 (n =85)	-2.47 (± 2.640)			
Change at Month 27 (n =83)	-2.65 (± 2.658)			
Change at Month 30 (n =82)	-2.95 (± 2.672)			
Change at Month 33 (n =80)	-2.85 (± 2.671)			
Change at Month 36 (n =71)	-2.88 (± 2.521)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects With Presence of Spondylitis at Screening and Baseline BASDAI Score >=4 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point title	Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects With Presence of Spondylitis at Screening and Baseline BASDAI Score >=4 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point description:

BASDAI was a validated self-assessment tool used to determine disease activity in subjects with ankylosing spondylitis. Utilizing a VAS of 0-10 cm (0= none and 10= very severe) subjects answered 6 questions pertaining to 5 symptoms including fatigue, spinal pain, joint pain/swelling, areas of localized tenderness and morning stiffness. The final BASDAI score was an average of answers to 6 questions, with an overall possible score range of 0 to 10 cm with higher score represented more severe ankylosing spondylitis disease activity. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with presence of spondylitis at screening and baseline BASDAI score >=4 cm. n =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: centimeter				
arithmetic mean (standard deviation)				
Change at Month 1 (n =106)	-2.59 (± 2.324)			
Change at Month 3 (n =103)	-2.41 (± 2.227)			
Change at Month 6 (n =98)	-2.74 (± 2.350)			
Change at Month 9 (n =93)	-2.63 (± 2.175)			
Change at Month 12 (n =92)	-2.65 (± 2.364)			

Change at Month 15 (n =87)	-2.65 (± 2.487)			
Change at Month 18 (n =84)	-2.65 (± 2.652)			
Change at Month 21 (n =80)	-2.47 (± 2.602)			
Change at Month 24 (n =76)	-2.72 (± 2.616)			
Change at Month 27 (n =74)	-2.90 (± 2.640)			
Change at Month 30 (n =73)	-3.27 (± 2.596)			
Change at Month 33 (n =71)	-3.17 (± 2.589)			
Change at Month 36 (n =65)	-3.08 (± 2.459)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains were aggregated into two summary scores known as the physical component summary (PCS) score and the mental component summary (MCS) score. Norm-based domain scores, PCS and MCS scores were used in the analyses; each of which has a population mean of 50 with a standard deviation (SD) of 10 points, and ranges from minus infinity to plus infinity. A higher PCS score represented better physical health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =668)	6.44 (± 8.285)			
Change at Month 6 (n =630)	6.71 (± 8.496)			
Change at Month 12 (n =578)	7.23 (± 8.257)			
Change at Month 18 (n =534)	7.44 (± 8.729)			
Change at Month 24 (n =502)	7.79 (± 9.055)			
Change at Month 30 (n =471)	8.06 (± 8.899)			

Change at Month 36 (n =384)	7.77 (± 9.074)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains were aggregated into two summary scores known as the PCS score and the MCS score. Norm-based domain scores, PCS and MCS scores were used in the analyses; each of which has a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher MCS score represents better mental health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =668)	4.72 (± 10.480)			
Change at Month 6 (n =630)	4.98 (± 11.052)			
Change at Month 12 (n =578)	5.25 (± 11.072)			
Change at Month 18 (n =534)	5.53 (± 11.055)			
Change at Month 24 (n =502)	5.79 (± 11.122)			
Change at Month 30 (n =471)	5.82 (± 11.726)			
Change at Month 36 (n =384)	6.18 (± 11.284)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

SF-36v2 was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 10 items of the physical functioning scale represented levels and kinds of limitations between extremes of physical activities, including lifting & carrying groceries; climbing stairs; bending, kneeling, or stooping; walking moderate distances; self-care limitations. The physical functioning items capture the presence & extent of physical limitations using a 3-level response continuum. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher physical functioning domain score represented better physical functioning. FAS of main study was analyzed. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	6.06 (± 9.425)			
Change at Month 6 (n =635)	6.44 (± 9.834)			
Change at Month 12 (n =582)	7.00 (± 9.472)			
Change at Month 18 (n =536)	7.31 (± 9.891)			
Change at Month 24 (n =505)	7.69 (± 10.280)			
Change at Month 30 (n =472)	7.96 (± 10.146)			
Change at Month 36 (n =386)	7.80 (± 10.703)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

SF-36v2 acute was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 4-item role-

physical scale covers an array of physical health-related role limitations, including: a) limitations in the kind of work or other usual activities; b) reductions in the amount of time spent on work or other usual activities; c) difficulty performing work or other usual activities; & d) accomplishing less. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher role-physical domain score represented better role-physical functioning. FAS of main study was analyzed. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =669)	6.19 (± 9.545)			
Change at Month 6 (n =631)	6.56 (± 9.650)			
Change at Month 12 (n =579)	6.61 (± 9.293)			
Change at Month 18 (n =534)	7.07 (± 10.050)			
Change at Month 24 (n =503)	7.46 (± 10.094)			
Change at Month 30 (n =473)	7.64 (± 10.041)			
Change at Month 36 (n =384)	7.40 (± 9.996)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The bodily pain scale comprises of 2 items pertaining to the intensity of bodily pain and extent of interference with normal work activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher bodily pain domain score represented less bodily pain. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =673)	8.36 (± 9.797)			
Change at Month 6 (n =636)	8.52 (± 10.033)			
Change at Month 12 (n =582)	9.29 (± 9.777)			
Change at Month 18 (n =536)	9.70 (± 10.271)			
Change at Month 24 (n =504)	9.95 (± 10.980)			
Change at Month 30 (n =473)	10.21 (± 10.645)			
Change at Month 36 (n =386)	10.45 (± 10.627)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The general health scale consisted of 5 items including a rating of health and 4 items addressing the respondent's view and expectations of his or her health. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher general health domain score represented better general health perceptions. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	3.89 (± 8.033)			
Change at Month 6 (n =636)	4.09 (± 8.640)			
Change at Month 12 (n =582)	4.68 (± 8.652)			
Change at Month 18 (n =536)	4.76 (± 8.386)			
Change at Month 24 (n =504)	4.89 (± 8.608)			
Change at Month 30 (n =473)	4.81 (± 8.590)			
Change at Month 36 (n =386)	4.36 (± 8.847)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 4-item measure of vitality captures a broad range of subjective evaluations of well-being from feelings of tiredness and being worn out to feeling full of energy all or most of the time. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher vitality domain score represents better vitality. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	5.92 (± 10.160)			
Change at Month 6 (n =636)	6.03 (± 10.546)			
Change at Month 12 (n =582)	6.72 (± 10.367)			
Change at Month 18 (n =536)	6.67 (± 10.147)			

Change at Month 24 (n =504)	7.10 (± 10.828)			
Change at Month 30 (n =474)	7.62 (± 10.808)			
Change at Month 36 (n =386)	7.65 (± 10.403)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 2-item social functioning scale assessed health-related effects on quantity and quality of social activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher social functioning domain score represented better social functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	6.08 (± 11.028)			
Change at Month 6 (n =636)	6.51 (± 10.923)			
Change at Month 12 (n =582)	7.16 (± 10.932)			
Change at Month 18 (n =536)	6.76 (± 11.272)			
Change at Month 24 (n =504)	7.28 (± 11.487)			
Change at Month 30 (n =473)	7.64 (± 11.597)			
Change at Month 36 (n =386)	7.83 (± 11.977)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Emotional Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Emotional Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 3-item role-emotional scale assessed mental health-related role limitations in terms of a) time spent in work or other usual activities; b) amount of work or activities accomplished; c) care with which work or other activities were performed. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher role-emotional domain score represented better role-emotional functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =668)	5.40 (± 11.962)			
Change at Month 6 (n =632)	5.39 (± 12.445)			
Change at Month 12 (n =578)	5.73 (± 12.235)			
Change at Month 18 (n =534)	6.71 (± 12.647)			
Change at Month 24 (n =502)	6.82 (± 12.154)			
Change at Month 30 (n =473)	6.54 (± 12.843)			
Change at Month 36 (n =384)	6.95 (± 12.859)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Short-Form-36 Health

	Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 5-item mental health scale includes 1 or more items from each of 4 major mental health dimensions: anxiety, depression, loss of behavioral/emotional control, and psychological well-being. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher mental health domain score represented better mental health functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	4.85 (± 10.306)			
Change at Month 6 (n =636)	5.39 (± 10.893)			
Change at Month 12 (n =582)	5.56 (± 10.781)			
Change at Month 18 (n =536)	5.82 (± 10.730)			
Change at Month 24 (n =504)	6.09 (± 11.247)			
Change at Month 30 (n =474)	6.18 (± 11.278)			
Change at Month 36 (n =386)	6.37 (± 11.199)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol- 5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol- 5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L mobility domain score were reported in this outcome measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	-0.24 (± 0.529)			
Change at Month 6 (n =635)	-0.30 (± 0.540)			
Change at Month 12 (n =582)	-0.28 (± 0.511)			
Change at Month 18 (n =536)	-0.30 (± 0.538)			
Change at Month 24 (n =505)	-0.31 (± 0.545)			
Change at Month 30 (n =474)	-0.30 (± 0.526)			
Change at Month 36 (n =386)	-0.32 (± 0.555)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L self-care domain score were reported in this outcome measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =673)	-0.19 (± 0.547)			
Change at Month 6 (n =633)	-0.20 (± 0.530)			
Change at Month 12 (n =581)	-0.19 (± 0.532)			
Change at Month 18 (n =535)	-0.21 (± 0.522)			
Change at Month 24 (n =503)	-0.21 (± 0.534)			
Change at Month 30 (n =473)	-0.23 (± 0.533)			
Change at Month 36 (n =385)	-0.24 (± 0.589)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L usual activities domain score were reported in this measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	-0.27 (± 0.588)			
Change at Month 6 (n =635)	-0.30 (± 0.539)			

Change at Month 12 (n =582)	-0.33 (± 0.547)			
Change at Month 18 (n =536)	-0.32 (± 0.579)			
Change at Month 24 (n =505)	-0.36 (± 0.547)			
Change at Month 30 (n =474)	-0.34 (± 0.571)			
Change at Month 36 (n =386)	-0.35 (± 0.594)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L pain/discomfort domain score were reported in this endpoint. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	-0.31 (± 0.557)			
Change at Month 6 (n =635)	-0.32 (± 0.570)			
Change at Month 12 (n =582)	-0.36 (± 0.568)			
Change at Month 18 (n =536)	-0.40 (± 0.584)			
Change at Month 24 (n =505)	-0.41 (± 0.602)			
Change at Month 30 (n =474)	-0.41 (± 0.601)			
Change at Month 36 (n =386)	-0.40 (± 0.613)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L anxiety/depression domain score were reported in this endpoint. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	-0.23 (± 0.600)			
Change at Month 6 (n =635)	-0.26 (± 0.623)			
Change at Month 12 (n =582)	-0.25 (± 0.594)			
Change at Month 18 (n =536)	-0.26 (± 0.604)			
Change at Month 24 (n =505)	-0.29 (± 0.605)			
Change at Month 30 (n =473)	-0.31 (± 0.608)			
Change at Month 36 (n =386)	-0.29 (± 0.651)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

The EQ VAS recorded the subject's self-rated health on a vertical VAS as standard vertical 0 (worst imaginable health state) to 100 mm (best imaginable health state) (similar to a thermometer) for recording an individual's rating for their current health-related quality of life state; higher score indicated a better health state. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: millimeter				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	14.12 (± 24.928)			
Change at Month 6 (n =636)	15.71 (± 25.871)			
Change at Month 12 (n =582)	16.00 (± 24.896)			
Change at Month 18 (n =535)	16.68 (± 24.746)			
Change at Month 24 (n =505)	17.43 (± 25.226)			
Change at Month 30 (n =473)	17.87 (± 25.363)			
Change at Month 36 (n =386)	18.07 (± 25.185)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less

daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired);3)change in FACIT-F total score(0-52)= Summing 13 items,higher score indicated lower level of fatigue, better subject status.All responses added with equal weight to get total score.FAS.n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	7.0 (± 9.78)			
Change at Month 6 (n =636)	7.7 (± 10.13)			
Change at Month 12 (n =582)	7.8 (± 9.70)			
Change at Month 18 (n =536)	8.1 (± 10.06)			
Change at Month 24 (n =506)	8.3 (± 10.61)			
Change at Month 30 (n =474)	8.7 (± 10.93)			
Change at Month 36 (n =386)	9.1 (± 11.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 6, 12, 18, 24, 30 and 36

End point title	Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 6, 12, 18, 24, 30 and 36

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired);3)change in FACIT-F total score(0-52)= Summing 13 items,higher score indicated lower level of fatigue, better subject status.All responses added with equal weight to get total score.FAS.n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =674)	3.1 (± 4.47)			
Change at Month 6 (n =636)	3.4 (± 4.61)			
Change at Month 12 (n =582)	3.5 (± 4.48)			
Change at Month 18 (n =536)	3.6 (± 4.63)			
Change at Month 24 (n =506)	3.7 (± 4.93)			
Change at Month 30 (n =474)	3.9 (± 5.02)			
Change at Month 36 (n =386)	4.0 (± 4.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point title	Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue,better subject status)=summing 13 items,all responses added with equal weight to get total score.FAS. n=subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

End point values	Tofacitinib			
Subject group type	Reporting group			
Number of subjects analysed	686			
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n= 674)	3.9 (± 5.98)			
Change at Month 6 (n= 636)	4.2 (± 6.19)			
Change at Month 12 (n= 582)	4.4 (± 5.88)			
Change at Month 18 (n= 536)	4.5 (± 6.05)			
Change at Month 24 (n= 506)	4.6 (± 6.34)			
Change at Month 30 (n= 474)	4.8 (± 6.46)			

Change at Month 36 (n= 386)	5.0 (± 6.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 9 and 12

End point title	Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 9 and 12

End point description:

HAQ-DI assesses the degree of difficulty a subject has experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain score and divided by the number of domains answered. Total possible score range 0 (least difficulty) and 3 (extreme difficulty), where higher score indicate more difficulty while performing daily living activities. FAS for sub-study included all subjects who were randomized to the sub-study and received at least 1 dose of (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.0164 (± 0.02438)	0.0322 (± 0.02411)		
Change at Month 3	0.0057 (± 0.02512)	0.0381 (± 0.02474)		
Change at Month 9	0.0720 (± 0.03195)	0.0663 (± 0.03125)		
Change at Month 12	0.0467 (± 0.02998)	0.0563 (± 0.02941)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of

treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.0486
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0192
upper limit	0.1163

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.0325
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0372
upper limit	0.1021

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.0058

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0941
upper limit	0.0825

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.0096
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0734
upper limit	0.0927

Secondary: Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Months 1, 3, 9 and 12

End point title	Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Months 1, 3, 9 and 12

End point description:

PASDAS was composite PsA disease activity score that included following components:Physician and patient global assessment of disease activity (assessed on a 0-100 VAS) in mm, swollen (66 joints) and tender joint counts (68 joints), Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6), tender dactylitic digit score (scored on a scale of 0-3, where 0= no tenderness and 3= extreme tenderness), SF-36 physical component summary (norm-based domain score were used in analyses; with a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity) and RP in mg/L. PASDAS was composite score and was a weighted index with score range of 0 to 10, where higher score indicated more severe disease. FAS of sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.000 (± 0.0701)	0.032 (± 0.0696)		
Change at Month 3	0.188 (± 0.0869)	0.165 (± 0.0868)		
Change at Month 9	0.158 (± 0.0934)	0.371 (± 0.0912)		
Change at Month 12	0.194 (± 0.0898)	0.133 (± 0.0882)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.032
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.163
upper limit	0.227

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.024

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.266
upper limit	0.219

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	0.213
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.47

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean Difference
Point estimate	-0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.309
upper limit	0.188

Secondary: Sub-study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC) at Months 1, 3, 6, 9 and 12

End point description:

PsARC was comprised of 4 clinical improvement criteria: >=20% improvement in PhyGA, >=20% improvement in PtGA; and >=30% reduction in the number of tender joints; and >=30% reduction in the number of swollen joints. PtGA: subject assessed health on VAS, 0 mm (very well) to 100 mm (worst health condition), higher score = worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. To achieve a clinical response, the subject must improve in 2 of the 4 PsARC criteria, 1 of which has to be the number of tender or swollen joints and none of the 4 score could worsen. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: percentage of subjects				
number (not applicable)				
Month 1	12.36	12.22		
Month 3	11.24	6.67		
Month 6	12.36	6.67		
Month 9	12.36	10.00		
Month 12	13.48	3.33		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.76
upper limit	9.48

	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis title	
Statistical analysis description: Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of subjects
Point estimate	-4.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.91
upper limit	3.77

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	-5.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.26
upper limit	2.87

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	-2.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.59
upper limit	6.87

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	-10.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.16
upper limit	-2.14

Secondary: Sub-study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects With Baseline PGA-PsO Score >0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects With Baseline PGA-PsO Score >0) at Months 1, 3, 6, 9 and 12

End point description:

The PGA-PsO was a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling were scored separately over the whole body according to a 5-point severity scale (0-4). Higher score indicated higher disease severity. Severity score for each erythema, induration and scaling were summed and averaged after which the total average was rounded to the nearest whole number score to determine a PGA-PsO score on a scale of 0 to 4 (0= clear, except for any residual discoloration, 1= almost clear, 2= mild, 3= moderate, 4= severe). Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline PGA-PsO score >0.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	33		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.1 (± 0.10)	0.2 (± 0.11)		
Change at Month 3	-0.1 (± 0.12)	0.1 (± 0.14)		
Change at Month 6	-0.1 (± 0.11)	0.2 (± 0.12)		
Change at Month 9	-0.3 (± 0.13)	0.2 (± 0.13)		
Change at Month 12	0.0 (± 0.15)	0.3 (± 0.15)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.8

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.7

Secondary: Sub-study: Percent Change from Baseline in Body Surface Area (BSA) (For Subjects With BSA >0%) With Psoriasis at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Percent Change from Baseline in Body Surface Area (BSA) (For Subjects With BSA >0%) With Psoriasis at Months 1, 3, 6, 9 and 12

End point description:

Assessment of BSA with psoriasis was estimated by means of handprint method, where full palmar hand of subject (fully extended palm, fingers and thumb together) represented approximately 1% of total BSA. Body regions are assigned specific number of handprints with percentage (Head and neck = 10 handprints [1 handprint =10%], upper extremities = 20 handprints [1 handprint =5%], Trunk (including axillae and groin) = 30 handprints [1 handprint =3.33%], lower extremities (including buttocks) = 40 handprints [1 handprint =2.5%]. Number of handprints of psoriatic skin in a body region was used to determine extent (%) to which a body region was involved with psoriasis. Total BSA affected was summation of individual regions affected. Analysis population included all subjects who were randomized to sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline body surface Area >0. "n'' =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	42		
Units: percent change				
least squares mean (standard error)				
At Month 1 (n =44, 42)	28.47 (± 13.497)	9.04 (± 13.972)		
At Month 3 (n =44, 41)	43.58 (± 18.679)	13.47 (± 19.348)		
At Month 6 (n =42, 41)	41.51 (± 20.745)	17.19 (± 21.157)		
At Month 9 (n =40, 40)	35.36 (± 17.309)	23.72 (± 17.691)		
At Month 12 (n =39, 38)	34.74 (± 19.909)	41.75 (± 20.333)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

At Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-19.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.06
upper limit	19.21

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

At Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-30.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-83.58
upper limit	23.37

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

At Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-24.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-83.35
upper limit	34.69

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

At Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-11.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.87
upper limit	37.58

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

At Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	7.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.73
upper limit	63.77

Secondary: Sub-study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects with Baseline DSS >0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects with Baseline DSS >0) at Months 1, 3, 6, 9 and 12

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis score for a subject was 0-60. Higher score indicated greater degree of tenderness. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline DSS >0. 99999 =SD could not be estimated because only 1 subjects was analyzed. "n'' =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Month 1 (n =7, 1)	-0.4 (± 0.79)	0.0 (± 99999)		
Change at Month 3 (n =6, 1)	-0.3 (± 0.52)	-1.0 (± 99999)		
Change at Month 6 (n =6, 1)	-0.3 (± 0.52)	-1.0 (± 99999)		
Change at Month 9 (n =6, 1)	-0.3 (± 0.52)	-1.0 (± 99999)		
Change at Month 12(n =6, 1)	-0.3 (± 0.52)	-1.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Percentage of Subjects with Absence of Dactylitis (For Subjects With Baseline DSS >0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Percentage of Subjects with Absence of Dactylitis (For Subjects With Baseline DSS >0) at Months 1, 3, 6, 9 and 12

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis score for a subject was 0-60. Higher score indicated greater degree of tenderness. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline DSS >0.

End point type	Secondary

End point timeframe:

Sub-study: Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	1		
Units: percentage of subjects				
number (not applicable)				
Month 1	14.29	0.0		
Month 3	14.29	0.0		
Month 6	14.29	0.0		
Month 9	14.29	0.0		
Month 12	14.29	0.0		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	6.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.58
upper limit	72.08

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	6.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.58
upper limit	72.08

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	6.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.58
upper limit	72.08

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	6.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.58
upper limit	72.08

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	6.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.58
upper limit	72.08

Secondary: Sub-study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and Achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline Leeds enthesitis index >0. "n'' =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1 (n =15, 16)	-0.2 (± 0.25)	-0.4 (± 0.24)		
Change at Month 3 (n =15, 15)	-0.3 (± 0.23)	-0.5 (± 0.23)		
Change at Month 6 (n =15, 16)	-0.5 (± 0.29)	-0.7 (± 0.28)		
Change at Month 9 (n =15, 16)	-0.3 (± 0.29)	0.0 (± 0.28)		
Change at Month 12 (n =15, 15)	-0.5 (± 0.28)	-0.3 (± 0.27)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1

Secondary: Sub-study: Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI =0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI =0) at Months 1, 3, 6, 9 and 12

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and Achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline LEI =0. "n'' =subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Sub-study: Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 1 (n =72, 73)	0.2 (± 0.64)	0.1 (± 0.58)		
Month 3 (n =71, 72)	0.2 (± 0.56)	0.0 (± 0.24)		
Month 6 (n =69, 72)	0.2 (± 0.76)	0.2 (± 0.82)		
Month 9 (n =68, 71)	0.1 (± 0.24)	0.1 (± 0.46)		
Month 12 (n = 68, 70)	0.2 (± 0.67)	0.1 (± 0.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Percentage of Subjects With Absence of Enthesitis Assessed Using Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Percentage of Subjects With Absence of Enthesitis Assessed Using Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline LEI >0.

End point type	Secondary
End point timeframe:	
Sub-study: Months 1, 3, 6, 9 and 12	

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: percentage of subjects				
number (not applicable)				
Month 1	13.33	25.00		
Month 3	13.33	43.75		
Month 6	26.67	56.25		
Month 9	13.33	37.50		
Month 12	26.67	43.75		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	11.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.65
upper limit	38.98

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	30.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	60.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	29.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.46
upper limit	62.62

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description:	
Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	24.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.14
upper limit	53.47

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	17.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.96
upper limit	50.12

Secondary: Sub-study: Percentage of Subjects With Minimal Disease Activity (MDA) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Percentage of Subjects With Minimal Disease Activity (MDA) at Months 1, 3, 6, 9 and 12

End point description:

A psoriatic arthritis subject was considered with MDA if subject had >= 5 of 7 criteria: 1) tender/painful joint count <=1; (2) swollen joint count <=1; (3) BSA <=3%; (4) Patient Assessment of Arthritis Pain (VAS) <=15 mm; (5) PtGA (VAS) <=20 mm; (6) HAQ-DI score <=0.5; (7) tender entheseal points (using LEI) <=1. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: Percentage of subjects				
number (not applicable)				
Month 1	50.56	55.56		
Month 3	50.56	54.44		
Month 6	46.07	48.89		
Month 9	42.70	46.67		
Month 12	41.57	44.44		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	4.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.61
upper limit	19.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	3.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.74
upper limit	18.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	2.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	17.45

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	3.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.58
upper limit	18.52

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage of subjects
Point estimate	2.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.63
upper limit	17.37

Secondary: Sub-study: Change From Baseline in Tender/Painful Joint Count at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Tender/Painful Joint Count at Months 1, 3, 6, 9 and 12

End point description:

68 joints were assessed to determine joints that are considered tender or painful. Response to pressure/motion on each joint was assessed using the following scale: Present/Absent/Not Done/Done/Not Applicable (to be used for artificial or missing joints). The 68 joints assessed were: 1) Upper Body: temporomandibular, sternoclavicular, acromioclavicular. 2) Upper Extremity: shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (MCP I, II, III, IV, V), thumb interphalangeal (IP), proximal interphalangeals (PIP II, III, IV, V), distal interphalangeals (DIP II, III, IV, V). 3) Lower Extremity: hip, knee, ankle, tarsus (includes subtalar, transverse tarsal and tarsometatarsal considered as one unit), metatarsophalangeals (MTP I, II, III, IV, V), great toe IP, proximal and distal interphalangeals combined (PIP II, III, IV, V). FAS for sub-study was analyzed.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: tender/painful joints				
least squares mean (standard error)				
Change at Month 1	0.7 (± 0.37)	0.3 (± 0.37)		
Change at Month 3	1.3 (± 0.44)	0.9 (± 0.44)		
Change at Month 6	0.5 (± 0.37)	0.5 (± 0.37)		
Change at Month 9	0.4 (± 0.33)	0.4 (± 0.32)		
Change at Month 12	0.3 (± 0.32)	0.5 (± 0.32)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.8

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.9

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.1

Secondary: Sub-study: Change From Baseline in Swollen Joint Count at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Swollen Joint Count at Months 1, 3, 6, 9 and 12

End point description:

Joints were assessed for swelling using the following scale: Present/Absent/Not Done/Not Applicable (to be used for artificial or missing joints). Sixty-six (66) joints were assessed for swelling. The 66 joints assessed were: 1) Upper Body: temporomandibular, sternoclavicular, acromioclavicular. 2) Upper Extremity: shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (MCP I, II, III, IV, V), thumb interphalangeal (IP), proximal interphalangeals (PIP II, III, IV, V), distal interphalangeals (DIP II, III, IV, V). 3) Lower Extremity: knee, ankle, tarsus (includes subtalar, transverse tarsal and tarsometatarsal considered as one unit), metatarsophalangeals (MTP I, II, III, IV, V), great toe IP, proximal and distal interphalangeals combined (PIP II, III, IV, V). FAS for sub-study was analyzed.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: swollen joints				
least squares mean (standard error)				
Change at Month 1	-0.1 (± 0.14)	99999 (± 0.14)		
Change at Month 3	0.3 (± 0.21)	0.3 (± 0.21)		
Change at Month 6	0.1 (± 0.16)	0.1 (± 0.15)		
Change at Month 9	0.0 (± 0.17)	0.2 (± 0.17)		
Change at Month 12	0.1 (± 0.14)	0.0 (± 0.14)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.3

Secondary: Sub-study: Change From Baseline in Physician's Global Assessment of Arthritis (PhyGA) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Physician's Global Assessment of Arthritis (PhyGA) at Months 1, 3, 6, 9 and 12

End point description:

The investigator or qualified assessor assessed how the subject’s overall arthritis appeared at the time of the visit. This was an evaluation based on the subject’s disease signs, functional capacity and physical examination, and independent of the PtGA and Patient Assessment of Arthritis Pain. The investigator’s response was recorded using a 100 mm VAS where 0 =PSA not active at all and 100 =PSA extremely active. Higher score indicated more PSA. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: millimeter				
least squares mean (standard error)				
Change at Month 1	-0.42 (± 0.992)	-0.17 (± 0.981)		
Change at Month 3	1.98 (± 1.225)	2.76 (± 1.216)		
Change at Month 6	1.18 (± 0.983)	1.65 (± 0.966)		
Change at Month 9	1.18 (± 1.316)	3.35 (± 1.287)		
Change at Month 12	0.86 (± 1.127)	0.75 (± 1.111)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	3.02

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	4.18

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.26
upper limit	3.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	5.81

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.25
upper limit	3.01

Secondary: Sub-study: Change From Baseline in Patient's Global Assessment of Arthritis (PtGA) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Patient's Global Assessment of Arthritis (PtGA) at Months 1, 3, 6, 9 and 12

End point description:

Subjects answered: "Considering all the ways your arthritis affects you, how are you feeling today?" Subject's response were recorded using a 0 - 100 mm VAS where 0 =not affected at all and 100 =extremely affected. Higher score indicated worse condition due to PSA.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: millimeter				
least squares mean (standard error)				
Change at Month 1	1.35 (± 1.277)	-0.68 (± 1.264)		
Change at Month 3	2.11 (± 1.537)	1.68 (± 1.516)		
Change at Month	3.17 (± 1.725)	4.45 (± 1.690)		
Change at Month 9	2.63 (± 1.691)	3.27 (± 1.655)		
Change at Month 12	2.77 (± 1.629)	2.65 (± 1.602)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.58
upper limit	1.52

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.69
upper limit	3.84

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.48
upper limit	6.06

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX
Statistical analysis description: Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.	
Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.03
upper limit	5.32

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.64
upper limit	4.38

Secondary: Sub-study: Change From Baseline in Patient's Assessment of Arthritis Pain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Patient's Assessment of Arthritis Pain at Months 1, 3, 6, 9 and 12

End point description:

Subjects assessed the severity of their arthritis pain using a 100 millimeter (mm) VAS by placing a mark on the scale between 0 (no pain) and 100 (most severe pain), which corresponded to the magnitude of their pain. Higher scores indicated more severe pain. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo). Higher scores indicated more severe pain.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: millimeter				
least squares mean (standard error)				
Change at Month 1	-0.05 (± 1.383)	-1.16 (± 1.370)		
Change at Month 3	1.59 (± 1.394)	0.36 (± 1.380)		
Change at Month 6	3.12 (± 1.709)	4.07 (± 1.674)		
Change at Month 9	2.44 (± 1.780)	4.45 (± 1.741)		
Change at Month 12	2.69 (± 1.692)	3.35 (± 1.664)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.96
upper limit	2.74

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.11
upper limit	2.65

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.78
upper limit	5.69

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	6.93

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.03
upper limit	5.35

Secondary: Sub-study: Change From Baseline in C-Reactive Protein (CRP) at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in C-Reactive Protein (CRP) at Months 1, 3, 6, 9 and 12

End point description:

The test for CRP was a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: mg/L				
least squares mean (standard error)				
Change at Month 1	-0.1171 (± 0.71654)	-0.2706 (± 0.70892)		
Change at Month 3	-0.3625 (± 0.48088)	-0.9285 (± 0.47675)		
Change at Month 6	0.5354 (± 0.79954)	-0.2637 (± 0.78002)		
Change at Month 9	-0.3217 (± 0.59271)	-0.2591 (± 0.57983)		
Change at Month 12	-0.1005 (± 0.78650)	0.2667 (± 0.77230)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1535
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1444
upper limit	1.8374

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.566
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9054
upper limit	0.7735

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.7991
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.0053
upper limit	1.4071

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.0626
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5767
upper limit	1.7018

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.3672
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8107
upper limit	2.545

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains are aggregated into two summary scores known as the physical component summary (PCS) score and the mental component summary (MCS) score. Norm-based domain scores, PCS and MCS scores are used in the analyses; each of which has a population mean of 50 with a standard deviation (SD) of 10 points, and ranges from minus infinity to plus infinity. A higher PCS score represented better physical health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.55 (± 0.424)	-0.22 (± 0.419)		
Change at Month 3	-0.90 (± 0.492)	-0.57 (± 0.487)		
Change at Month 6	-0.65 (± 0.480)	-1.42 (± 0.466)		
Change at Month 9	-1.09 (± 0.607)	-1.85 (± 0.593)		
Change at Month 12	-1.52 (± 0.533)	-1.00 (± 0.523)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	1.51

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	1.69

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	0.55

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	0.91

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	2

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. An additional item measures health transition. The 8 health domains are aggregated into two summary scores known as the PCS score and the MCS score. Norm-based domain scores, PCS and MCS scores are used in the

analyses; each of which has a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher MCS score represents better mental health status. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.35 (± 0.630)	-0.11 (± 0.622)		
Change at Month 3	0.09 (± 0.642)	-0.77 (± 0.634)		
Change at Month 6	-0.23 (± 0.733)	-0.89 (± 0.713)		
Change at Month 9	-0.71 (± 0.749)	0.06 (± 0.731)		
Change at Month 12	-0.38 (± 0.694)	-0.47 (± 0.681)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	1.29

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.65
upper limit	0.92

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.68
upper limit	1.36

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	2.83

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	1.84

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 3, 6, 9 and 12

End point description:

SF-36v2 was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 10 items of the physical functioning scale represented levels and kinds of limitations between extremes of physical activities, including lifting & carrying groceries; climbing stairs; bending, kneeling, or stooping; walking moderate distances; self-care limitations. The physical functioning items capture the presence & extent of physical limitations using a 3-level response continuum. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher physical functioning domain score represented better physical functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.37 (± 0.472)	-0.15 (± 0.467)		
Change at Month 3	-0.50 (± 0.562)	-0.33 (± 0.556)		
Change at Month 6	-0.27 (± 0.586)	-0.80 (± 0.571)		
Change at Month 9	-1.43 (± 0.657)	-1.11 (± 0.643)		
Change at Month 12	-1.01 (± 0.676)	-1.02 (± 0.664)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	1.53

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	1.73

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	1.08

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	2.13

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	1.86

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 3, 6, 9 and 12

End point description:

SF-36v2 acute was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 4-item role-physical scale covers an array of physical health-related role limitations, including: a) limitations in the kind of work or other usual activities; b) reductions in the amount of time spent on work or other usual activities; c) difficulty performing work or other usual activities; & d) accomplishing less. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher role-physical domain score represented better role-physical functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.27 (± 0.561)	0.22 (± 0.555)		

Change at Month 3	-1.04 (± 0.626)	0.21 (± 0.619)		
Change at Month 6	-1.57 (± 0.585)	-0.87 (± 0.569)		
Change at Month 9	-0.64 (± 0.638)	-0.44 (± 0.624)		
Change at Month 12	-1.85 (± 0.646)	-0.12 (± 0.635)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	2.05

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	2.99

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	2.31

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	1.96

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	3.52

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The bodily pain scale comprises of 2 items pertaining to the intensity of bodily pain and extent of interference with normal work activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher bodily pain domain score represented less bodily pain. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.77 (± 0.617)	-0.06 (± 0.609)		
Change at Month 3	-1.59 (± 0.661)	-1.24 (± 0.652)		
Change at Month 6	-0.61 (± 0.686)	-2.42 (± 0.669)		
Change at Month 9	-1.29 (± 0.808)	-3.05 (± 0.790)		
Change at Month 12	-1.69 (± 0.719)	-1.99 (± 0.706)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	2.42

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	2.18

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	0.09

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	0.48

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.69

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The general health scale consisted of 5 items including a rating of health and 4 items addressing the respondent's view and expectations of his or her health. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher general health domain score represented better general health perceptions. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.20 (± 0.492)	-0.48 (± 0.487)		
Change at Month 3	0.34 (± 0.516)	-0.79 (± 0.511)		
Change at Month 6	0.24 (± 0.493)	-0.57 (± 0.481)		
Change at Month 9	-0.48 (± 0.562)	-0.46 (± 0.551)		
Change at Month 12	-0.32 (± 0.539)	-0.29 (± 0.530)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	0.69

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	0.31

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	0.56

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.54
upper limit	1.57

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	1.53

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 4-item measure of vitality captures a broad range of subjective evaluations of well-being from feelings of tiredness and being worn out to feeling full of energy all or most of the time. Norm-based domain

scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher vitality domain score represented better vitality. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.04 (± 0.614)	-0.39 (± 0.607)		
Change at Month 3	-0.26 (± 0.593)	-1.12 (± 0.586)		
Change at Month 6	0.01 (± 0.705)	-1.70 (± 0.687)		
Change at Month 9	-0.80 (± 0.645)	-1.27 (± 0.632)		
Change at Month 12	-1.04 (± 0.640)	-0.09 (± 0.629)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	1.35

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	0.79

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.66
upper limit	0.23

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.47

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	1.32

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	2.73

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 2-item social functioning scale assessed health-related effects on quantity and quality of social activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher social functioning domain score represented better social functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.99 (± 0.734)	-0.22 (± 0.726)		
Change at Month 3	-0.80 (± 0.750)	-1.18 (± 0.740)		
Change at Month 6	-1.16 (± 0.776)	-1.74 (± 0.757)		
Change at Month 9	-1.50 (± 0.753)	-1.22 (± 0.737)		
Change at Month 12	-1.81 (± 0.758)	-1.28 (± 0.746)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	2.82

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.46
upper limit	1.71

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.72
upper limit	1.57

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	2.36

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	2.63

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role Emotional Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role Emotional Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 3-item role-emotional scale assessed mental health-related role limitations in terms of a) time spent in work or other usual activities; b) amount of work or activities accomplished; c) care with which work or other activities were performed. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher role-emotional domain score represented better role-emotional functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	1.14 (± 0.716)	-0.53 (± 0.707)		

Change at Month 3	0.24 (± 0.807)	-0.38 (± 0.797)		
Change at Month 6	-0.72 (± 0.788)	-0.82 (± 0.769)		
Change at Month 9	-0.78 (± 0.803)	-0.06 (± 0.782)		
Change at Month 12	-0.33 (± 0.835)	-1.11 (± 0.820)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.67
upper limit	0.32

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.86
upper limit	1.63

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.27
upper limit	2.09

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	2.95

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.53

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 3, 6, 9 and 12

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 5-item mental health scale includes 1 or more items from each of 4 major mental health dimensions: anxiety, depression, loss of behavioral/emotional control, and psychological well-being. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher mental health domain score represented better mental health functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.30 (± 0.676)	0.63 (± 0.669)		
Change at Month 3	-0.42 (± 0.661)	-0.31 (± 0.653)		
Change at Month 6	-0.01 (± 0.780)	-0.26 (± 0.762)		
Change at Month 9	-0.72 (± 0.724)	0.35 (± 0.710)		
Change at Month 12	-0.37 (± 0.723)	0.01 (± 0.711)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	2.81

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.72
upper limit	1.95

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	1.9

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	3.07

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	2.38

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 3, 6, 9 and 12

End point description:

FACIT-F:13-item questionnaire,with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52):calculated by summing 13 items,higher score indicated lower level of fatigue, better subject status. All responses were added with equal weight to get total score. FAS of sub-study.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-1.9 (± 0.61)	-1.1 (± 0.61)		
Change at Month 3	-1.8 (± 0.59)	-1.3 (± 0.58)		
Change at Month 6	-1.3 (± 0.61)	-2.0 (± 0.60)		
Change at Month 9	-2.1 (± 0.65)	-1.0 (± 0.64)		
Change at Month 12	-1.4 (± 0.66)	-0.7 (± 0.64)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.5

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2.9

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.6

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 3, 6, 9 and 12

End point description:

FACIT-F:13-item questionnaire, with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],

felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue, better subject status):calculated by summing 13 items,all responses were added with equal weight to get total score.FAS of sub-study was analyzed.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-0.9 (± 0.29)	-0.5 (± 0.29)		
Change at Month 3	-0.8 (± 0.31)	-0.9 (± 0.30)		
Change at Month 6	-0.5 (± 0.29)	-1.3 (± 0.28)		
Change at Month 9	-0.7 (± 0.31)	-0.8 (± 0.30)		
Change at Month 12	-0.5 (± 0.31)	-0.5 (± 0.31)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.7

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 3, 6, 9 and 12

End point description:

FACIT-F:13-item questionnaire, with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue, better subject status):calculated by summing 13 items,all responses were added with equal weight to get total score.FAS of sub-study was analyzed.

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	-1.1 (± 0.39)	-0.6 (± 0.39)		
Change at Month 3	-1.1 (± 0.35)	-0.4 (± 0.35)		
Change at Month 6	-0.8 (± 0.41)	-0.7 (± 0.40)		
Change at Month 9	-1.4 (± 0.42)	-0.2 (± 0.41)		
Change at Month 12	-0.9 (± 0.40)	-0.1 (± 0.40)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.7

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2.3

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.9

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 3, 6, 9 and 12

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L mobility domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.0 (± 0.04)	0.0 (± 0.04)		
Change at Month 3	0.0 (± 0.04)	0.0 (± 0.04)		
Change at Month 6	0.0 (± 0.04)	0.1 (± 0.04)		
Change at Month 9	0.0 (± 0.04)	0.1 (± 0.04)		
Change at Month 12	0.0 (± 0.04)	0.1 (± 0.04)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 3, 6, 9 and 12

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L self-care domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.0 (± 0.03)	0.0 (± 0.03)		
Change at Month 3	0.0 (± 0.03)	0.0 (± 0.03)		
Change at Month 6	0.0 (± 0.04)	0.0 (± 0.03)		
Change at Month 9	0.0 (± 0.04)	0.0 (± 0.04)		
Change at Month 12	0.0 (± 0.04)	0.1 (± 0.04)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 3, 6, 9 and 12

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L usual activities domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.0 (± 0.04)	0.0 (± 0.04)		
Change at Month 3	0.0 (± 0.04)	0.0 (± 0.04)		
Change at Month 6	0.0 (± 0.04)	0.1 (± 0.04)		
Change at Month 9	0.1 (± 0.04)	0.1 (± 0.04)		
Change at Month 12	0.0 (± 0.04)	0.0 (± 0.04)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 3, 6, 9 and 12

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L pain/discomfort domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.1 (± 0.04)	0.0 (± 0.04)		
Change at Month 3	0.1 (± 0.04)	0.1 (± 0.04)		
Change at Month 6	0.1 (± 0.04)	0.1 (± 0.04)		
Change at Month 9	0.1 (± 0.05)	0.1 (± 0.05)		

Change at Month 12	0.1 (± 0.05)	0.2 (± 0.05)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 3, 6, 9 and 12

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L anxiety/depression domain score were reported in this endpoint. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: units on a scale				
least squares mean (standard error)				
Change at Month 1	0.1 (± 0.04)	0.0 (± 0.04)		
Change at Month 3	0.0 (± 0.05)	0.0 (± 0.04)		
Change at Month 6	0.1 (± 0.05)	0.0 (± 0.05)		
Change at Month 9	0.1 (± 0.05)	0.0 (± 0.05)		
Change at Month 12	0.1 (± 0.05)	0.0 (± 0.05)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0

Secondary: Sub-study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 3, 6, 9 and 12

End point title	Sub-study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 3, 6, 9 and 12

End point description:

The EQ VAS recorded the subject's self-rated health on a vertical VAS as standard verticle 0 (worst imaginable health state) to 100 mm (best imaginable health state) (similar to a thermometer) for recording an individual's rating for their current health-related quality of life state; higher score indicated a better health state. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

End point type	Secondary

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

End point values	Tofacitinib 5 mg BID + Methotrexate (MTX)	Tofacitinib 5 mg BID + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	90		
Units: millimeter				
least squares mean (standard error)				
Change at Month 1	2.0 (± 1.19)	-0.9 (± 1.16)		
Change at Month 3	0.5 (± 1.54)	-1.1 (± 1.52)		
Change at Month 6	4.4 (± 1.41)	-1.9 (± 1.38)		
Change at Month 9	2.5 (± 1.59)	-0.4 (± 1.56)		
Change at Month 12	3.0 (± 1.82)	-1.9 (± 1.78)		

Statistical analyses

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	0.4

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	2.7

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	-2.4

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	1.6

Statistical analysis title	Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

Comparison groups	Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean difference
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	0.2

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day 1) up to last dose of main study (maximum up to 36 months) if not enrolled into sub-study or from baseline up to last dose of sub-study (maximum up to 48 months) if enrolled into sub-study

Adverse event reporting additional description:

As pre-specified in protocol/SAP, safety data were planned to be assessed as a single group in main study. For main study, analysis of safety data included cumulative data from main and sub-study as single group. Safety data collected in sub-study was analyzed for tofacitinib 5 mg BID + MTX and tofacitinib 5 mg BID + placebo, separately.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	All Tofacitinib

Reporting group description:

Main Study: Subjects with active PsA received tofacitinib 5 mg oral tablet, BID with or without allowed concomitant DMARDs examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion. Sub-study: Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX capsules orally (dose range from 7.5 to 20 mg per week) or tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules, for up to 12 months.

Reporting group title	Tofacitinib 5 mg BID + Placebo

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months.

Reporting group title	Tofacitinib 5 mg BID + Methotrexate (MTX)

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months.

Serious adverse events	All Tofacitinib	Tofacitinib 5 mg BID + Placebo	Tofacitinib 5 mg BID + Methotrexate (MTX)
Total subjects affected by serious adverse events			
subjects affected / exposed	115 / 686 (16.76%)	4 / 90 (4.44%)	3 / 89 (3.37%)
number of deaths (all causes)	6	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			

subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 686 (0.15%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myelomonocytic leukaemia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medullary thyroid cancer			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleomorphic adenoma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post thrombotic syndrome			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nodule			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Miscarriage of partner			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast disorder female			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ovarian cyst			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meconium aspiration syndrome			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Bipolar I disorder			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar disorder			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device loosening			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Heart rate decreased			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cartilage injury			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chemical poisoning			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			

subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	1 / 686 (0.15%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	3 / 686 (0.44%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prinzmetal angina			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 686 (0.15%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			

Deafness neurosensory			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn’s disease			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Incarcerated umbilical hernia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal prolapse			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary retention			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	4 / 686 (0.58%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Joint swelling			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	7 / 686 (1.02%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	1 / 686 (0.15%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			

subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral lateral recess stenosis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV infection			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 686 (0.29%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyoderma			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serratia sepsis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia herpes viral			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cardiometabolic syndrome			

subjects affected / exposed	1 / 686 (0.15%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	All Tofacitinib	Tofacitinib 5 mg BID + Placebo	Tofacitinib 5 mg BID + Methotrexate (MTX)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	457 / 686 (66.62%)	24 / 90 (26.67%)	25 / 89 (28.09%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	34 / 686 (4.96%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	45	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 686 (3.06%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	23	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	36 / 686 (5.25%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	44	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	22 / 686 (3.21%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	28	0	0
Hepatic enzyme increased			
subjects affected / exposed	15 / 686 (2.19%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	19	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	24 / 686 (3.50%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	24	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	50 / 686 (7.29%)	2 / 90 (2.22%)	2 / 89 (2.25%)
occurrences (all)	52	2	2
Nervous system disorders			

Dizziness			
subjects affected / exposed	20 / 686 (2.92%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	22	0	0
Headache			
subjects affected / exposed	32 / 686 (4.66%)	0 / 90 (0.00%)	2 / 89 (2.25%)
occurrences (all)	45	0	2
Sciatica			
subjects affected / exposed	19 / 686 (2.77%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	24	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 686 (2.19%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	15	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	14 / 686 (2.04%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	14	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	25 / 686 (3.64%)	3 / 90 (3.33%)	0 / 89 (0.00%)
occurrences (all)	35	4	0
Abdominal pain upper			
subjects affected / exposed	17 / 686 (2.48%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	19	0	0
Dyspepsia			
subjects affected / exposed	15 / 686 (2.19%)	0 / 90 (0.00%)	2 / 89 (2.25%)
occurrences (all)	17	0	2
Nausea			
subjects affected / exposed	27 / 686 (3.94%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	32	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	17 / 686 (2.48%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	22	0	0
Oropharyngeal pain			

subjects affected / exposed	14 / 686 (2.04%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	16	0	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	32 / 686 (4.66%)	1 / 90 (1.11%)	2 / 89 (2.25%)
occurrences (all)	40	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	32 / 686 (4.66%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	44	0	0
Back pain			
subjects affected / exposed	31 / 686 (4.52%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	39	0	0
Psoriatic arthropathy			
subjects affected / exposed	44 / 686 (6.41%)	0 / 90 (0.00%)	3 / 89 (3.37%)
occurrences (all)	51	0	3
Intervertebral disc disorder			
subjects affected / exposed	0 / 686 (0.00%)	2 / 90 (2.22%)	0 / 89 (0.00%)
occurrences (all)	0	2	0
Osteoporosis			
subjects affected / exposed	0 / 686 (0.00%)	2 / 90 (2.22%)	0 / 89 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	67 / 686 (9.77%)	3 / 90 (3.33%)	2 / 89 (2.25%)
occurrences (all)	84	3	3
Gastroenteritis			
subjects affected / exposed	19 / 686 (2.77%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	25	0	0
Nasopharyngitis			
subjects affected / exposed	104 / 686 (15.16%)	3 / 90 (3.33%)	1 / 89 (1.12%)
occurrences (all)	172	4	2
Pharyngitis			
subjects affected / exposed	38 / 686 (5.54%)	3 / 90 (3.33%)	3 / 89 (3.37%)
occurrences (all)	48	3	3
Respiratory tract infection			

subjects affected / exposed	17 / 686 (2.48%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	32	0	0
Sinusitis			
subjects affected / exposed	33 / 686 (4.81%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	44	0	0
Upper respiratory tract infection			
subjects affected / exposed	124 / 686 (18.08%)	4 / 90 (4.44%)	6 / 89 (6.74%)
occurrences (all)	190	4	6
Urinary tract infection			
subjects affected / exposed	66 / 686 (9.62%)	4 / 90 (4.44%)	3 / 89 (3.37%)
occurrences (all)	92	5	5
Herpes zoster			
subjects affected / exposed	26 / 686 (3.79%)	1 / 90 (1.11%)	2 / 89 (2.25%)
occurrences (all)	27	1	2
Influenza			
subjects affected / exposed	19 / 686 (2.77%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	23	0	0
Oral herpes			
subjects affected / exposed	19 / 686 (2.77%)	1 / 90 (1.11%)	2 / 89 (2.25%)
occurrences (all)	37	2	4
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	14 / 686 (2.04%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences (all)	14	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2017	Protocol Summary updated to reflect new sub-study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported