Clinical trial results:
A Phase 3b/4 Randomized Double-Blind Study of 5 mg of Tofacitinib With and Without Methotrexate in Comparison to Adalimumab With Methotrexate in Subjects With Moderately to Severely Active Rheumatoid Arthritis

Summary

EudraCT number	2014-000358-13
Trial protocol	CZ EE LT LV GB ES PL BG RO DE HR
Global end of trial date	16 December 2016

Results information

Result version number	v1 (current)
This version publication date	06 December 2017
First version publication date	06 December 2017

Trial information

Trial identification

Sponsor protocol code	A3921187

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02187055
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to compare the efficacy of 5 mg twice daily (BID) of tofacitinib (with and without background methotrexate [MTX]) to adalimumab with MTX as measured by American College of Rheumatology (ACR) criteria 50% improvement (ACR50) response rates at Month 6 and to compare the efficacy of 5 mg BID tofacitinib monotherapy versus 5 mg BID tofacitinib with MTX as measured by ACR50 response rates at Month 6.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation Good Clinical Practice Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants. The final protocol and any amendments were reviewed and approved by the Institutional Review Board(s) and/or Independent Ethics Committee(s) at each of the investigational centres participating in the study.

Background therapy:

Throughout the study subjects were to continue on their stable background arthritis therapy, which included MTX (or placebo MTX) and folic acid supplement and could have included nonsteroidal anti-inflammatory drugs, selective cyclooxygenase 2 inhibitors, opioids, cetaminophen, and/or low dose oral corticosteroids (less than or equal to 10 mg prednisone or equivalent per day).

Evidence for comparator:

Adalimumab is a recombinant human immunoglobulin G1 monoclonal antibody specific for human tumor necrosis factor. It is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult subjects with moderately to severely active rheumatoid arthritis (RA). The currently approved dose is 40 mg every other week in adult subjects with RA.

Actual start date of recruitment	06 August 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	Argentina: 43
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Bosnia and Herzegovina: 36
Country: Number of subjects enrolled	Bulgaria: 56
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Chile: 16
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Estonia: 10
Country: Number of subjects enrolled	Israel: 12

Country: Number of subjects enrolled	Korea, Republic of: 37
Country: Number of subjects enrolled	Latvia: 4
Country: Number of subjects enrolled	Lithuania: 30
Country: Number of subjects enrolled	Mexico: 200
Country: Number of subjects enrolled	Peru: 17
Country: Number of subjects enrolled	Philippines: 43
Country: Number of subjects enrolled	Poland: 115
Country: Number of subjects enrolled	Romania: 46
Country: Number of subjects enrolled	Russian Federation: 111
Country: Number of subjects enrolled	South Africa: 60
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	Thailand: 15
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 201
Worldwide total number of subjects	1146
EEA total number of subjects	313

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)	992
From 65 to 84 years	152
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Confirmation of RA diagnosis and classification of RA was performed at the screening visit. Participants must have had a score of 6 or greater on the 2010 ACR/European League Against Rheumatism classification criteria for RA.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib 5 mg BID

Arm description:

One active tofacitinib 5 mg tablet orally BID plus placebo MTX (prior dose) orally every week plus placebo adalimumab 40 mg subcutaneously (SC) every other week for up to 12 months.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	CP-690550-10
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 active tofacitinib 5 mg tablet administered orally BID plus placebo MTX (prior dose) capsule(s) administered orally every week plus placebo adalimumab 40 mg injection administered subcutaneously (SC) every other week for up to 12 months.

Arm title	Tofacitinib 5 mg BID + MTX

Arm description:

One active tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus placebo adalimumab 40 mg SC every other week for up to 12 months.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib and methotrexate
Investigational medicinal product code	CP-690550-10
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 active tofacitinib 5 mg tablet administered orally BID plus active MTX (prior dose) capsule(s) administered orally every week plus placebo adalimumab 40 mg injection administered SC every other week for up to 12 months.

Arm title	Adalimumab 40 mg + MTX

Arm description:

One placebo tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus active adalimumab 40 mg SC every other week for up to 12 months.

Arm type	Active comparator

Investigational medicinal product name	Adalimumab and methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 placebo tofacitinib 5 mg tablet administered orally BID plus active MTX (prior dose) capsule(s) administered orally every week plus active adalimumab 40 mg injection administered SC every other week for up to 12 months.

Number of subjects in period 1	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX
Started	384	376	386
Completed	315	303	312
Not completed	69	73	74
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	11	11	11
Adverse event, non-fatal	21	26	36
No longer meets eligibility criteria	-	2	-
Pregnancy	3	1	-
No longer willing to participate	6	8	10
Unspecified	5	6	3
Lost to follow-up	2	7	3
Lack of efficacy	10	3	7
Protocol deviation	9	9	4

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
One active tofacitinib 5 mg tablet orally BID plus placebo MTX (prior dose) orally every week plus placebo adalimumab 40 mg subcutaneously (SC) every other week for up to 12 months.	
Reporting group title	Tofacitinib 5 mg BID + MTX
Reporting group description:	
One active tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus placebo adalimumab 40 mg SC every other week for up to 12 months.	
Reporting group title	Adalimumab 40 mg + MTX
Reporting group description:	
One placebo tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus active adalimumab 40 mg SC every other week for up to 12 months.	

Reporting group values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX
Number of subjects	384	376	386
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	335	332	325
From 65-84 years	49	42	61
85 years and over	0	2	0
Age Continuous Units: Years			
arithmetic mean	49.7	50.0	50.7
standard deviation	± 12.2	± 13.4	± 13.4
Gender, Male/Female Units: Subjects			
Female	319	311	320
Male	65	65	66

Reporting group values	Total		
Number of subjects	1146		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	992		
From 65-84 years	152		
85 years and over	2		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Subjects			
Female	950		
Male	196		

End points

End points reporting groups

Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
One active tofacitinib 5 mg tablet orally BID plus placebo MTX (prior dose) orally every week plus placebo adalimumab 40 mg subcutaneously (SC) every other week for up to 12 months.	
Reporting group title	Tofacitinib 5 mg BID + MTX
Reporting group description:	
One active tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus placebo adalimumab 40 mg SC every other week for up to 12 months.	
Reporting group title	Adalimumab 40 mg + MTX
Reporting group description:	
One placebo tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus active adalimumab 40 mg SC every other week for up to 12 months.	

Primary: Percentage of Participants Achieving American College of Rheumatology Criteria 50% Improvement (ACR50) Response at Month 6

End point title	Percentage of Participants Achieving American College of Rheumatology Criteria 50% Improvement (ACR50) Response at Month 6
End point description:	
ACR50 is a greater than or equal to (≥) 50 percent (%) improvement in tender joint count (TJC) or swollen joint count (SJC) and 50% improvement in 3 of the following 5 criteria: 1) physician's global assessment (PGA) of disease activity, 2) participant's assessment (PtGA) of disease activity, 3) participant's assessment of pain, 4) participant's assessment of functional disability via a health assessment questionnaire, and 5) C-reactive protein (CRP) at each visit.	
End point type	Primary
End point timeframe:	
Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	384	376	386	
Units: Percentage of participants				
number (not applicable)	38.28	46.01	43.78	

Statistical analyses

Statistical analysis title	Analysis of ACR50 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	760
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2101
Method	Normal approximation to proportions
Parameter estimate	Difference in response rate
Point estimate	-7.73
Confidence interval	
level	Other: 98.34 %
sides	2-sided
lower limit	-16.29
upper limit	0.83

Statistical analysis title	Analysis of ACR50 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	770
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0512
Method	Normal approximation to proportions
Parameter estimate	Difference in response rate
Point estimate	-5.5
Confidence interval	
level	Other: 98.34 %
sides	2-sided
lower limit	-13.98
upper limit	2.98

Statistical analysis title	Analysis of ACR50 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	762
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Normal approximation to proportions
Parameter estimate	Difference in response rate
Point estimate	2.23
Confidence interval	
level	Other: 98.34 %
sides	2-sided
lower limit	-6.4
upper limit	10.86

Secondary: Change from Baseline in Simplified Disease Activity Index (SDAI) Value

at Month 6

End point title	Change from Baseline in Simplified Disease Activity Index (SDAI) Value at Month 6

End point description:

SDAI is the numerical sum of five outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 centimeter (cm) visual analogue scale (VAS) (higher scores indicate greater affection due to disease activity), and CRP (mg/dL). SDAI total score ranges from 0 to 86. SDAI less than or equal to (≤) 3.3 indicates disease remission, >3.4 to 11 indicates low disease activity, >11 to 26 indicates moderate disease activity, and >26 indicates high disease activity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	355	343	345	
Units: Score on a scale				
least squares mean (standard error)	-23.7 (± 0.62)	-26.6 (± 0.62)	-25.6 (± 0.62)	

Statistical analyses

Statistical analysis title	Analysis of SDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	4.41

Statistical analysis title	Analysis of SDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	3.49

Statistical analysis title	Analysis of SDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	688
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.51
upper limit	0.68

Secondary: Change from Baseline in Clinical Disease Activity Index (CDAI) Value at Month 6

End point title	Change from Baseline in Clinical Disease Activity Index (CDAI) Value at Month 6

End point description:

CDAI is the numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76. CDAI ≤2.8 indicates disease remission, >2.8 to 10 indicates low disease activity, >10 to 22 indicates moderate disease activity, and >22 indicates high disease activity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	345	347	
Units: Score on a scale				
least squares mean (standard error)	-22.9 (± 0.61)	-25.5 (± 0.61)	-24.8 (± 0.61)	

Statistical analyses

Statistical analysis title	Analysis of CDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	4.18

Statistical analysis title	Analysis of CDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	3.48

Statistical analysis title	Analysis of CDAI at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	0.86

Secondary: Change from Baseline in Disease Activity Score 28-4 (DAS28-4) Including CRP at Month 6

End point title	Change from Baseline in Disease Activity Score 28-4 (DAS28-4) Including CRP at Month 6

End point description:

DAS28-4 (CRP) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and CRP (mg/L) using the following: DAS28-4(CRP) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP+1) + 0.014* PtGA (millimeters [mm]) + 0.96. Total score range: 0 to 9.4, higher score indicated higher disease activity. DAS28-4 (CRP) ≤3.2 indicates low disease activity, >3.2 to 5.1 indicates moderate to high disease activity, and less than (<) 2.6 indicates remission.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	355	343	345	
Units: Score on a scale				
least squares mean (standard error)	-2.1 (± 0.07)	-2.5 (± 0.07)	-2.3 (± 0.07)	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (CRP) at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.5

Statistical analysis title	Analysis of DAS28-4 (CRP) at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.39

Statistical analysis title	Analysis of DAS28-4 (CRP) at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	688
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.06

Secondary: Change from Baseline in Disease Activity Score 28-4 (DAS28-4) Including Erythrocyte Sedimentation Rate (ESR) at Month 6

End point title	Change from Baseline in Disease Activity Score 28-4 (DAS28-4) Including Erythrocyte Sedimentation Rate (ESR) at Month 6

End point description:

DAS28-4 (ESR) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and ESR (mm/hour) using the following: DAS28-4(ESR) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*ln(ESR) + 0.014* PtGA (mm). Total score range: 0 to 9.4, higher score indicated higher disease activity. DAS28-3 (ESR) ≤3.2 indicates low disease activity, >3.2 to 5.1 indicates moderate to high disease activity, and <2.6 indicates remission.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	349	342	343	
Units: Score on a scale				
least squares mean (standard error)	-2.1 (± 0.07)	-2.4 (± 0.07)	-2.4 (± 0.07)	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (ESR) at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	691
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.51

Statistical analysis title	Analysis of DAS28-4 (ESR) at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.46

Statistical analysis title	Analysis of DAS28-4 (ESR) at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	685
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.13

Secondary: Percentage of Participants Achieving Observed American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) Boolean Remission Criteria at Month 6

End point title	Percentage of Participants Achieving Observed American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) Boolean Remission Criteria at Month 6

End point description:

To meet the ACR-EULAR Boolean remission criteria, a participant must satisfy all of the following: TJC ≤1 and SJC ≤1 (both based on a 28-joint assessment), CRP ≤1 mg/dL, and PtGA ≤1 on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity).

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	358	346	355	
Units: Percentage of participants				
number (not applicable)	7.54	8.67	9.58	

Statistical analyses

Statistical analysis title	Analysis of Remission Criteria at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.99
upper limit	2.56

Statistical analysis title	Analysis of Remission Criteria at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	713
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.59
upper limit	2.04

Statistical analysis title	Analysis of Remission Criteria at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.53
upper limit	3.4

Secondary: Percentage of Participants Achieving SDAI ≤3.3 at Month 6

End point title	Percentage of Participants Achieving SDAI ≤3.3 at Month 6

End point description:

SDAI is the numerical sum of five outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity), and CRP (mg/dL). SDAI total score ranges from 0 to 86. SDAI ≤3.3 indicates disease remission.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	345	348	
Units: Percentage of participants				
number (not applicable)	10.64	13.91	14.37	

Statistical analyses

Statistical analysis title	Analysis of SDAI ≤3.3 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.95
upper limit	1.15

Statistical analysis title	Analysis of SDAI ≤3.3 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.55
upper limit	1.43

Statistical analysis title	Analysis of SDAI ≤3.3 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.45
upper limit	5.14

Secondary: Percentage of Participants Achieving CDAI ≤2.8 at Month 6

End point title	Percentage of Participants Achieving CDAI ≤2.8 at Month 6

End point description:

CDAI is the numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76. CDAI ≤2.8 indicates disease remission.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	358	347	350	
Units: Percentage of participants				
number (not applicable)	10.89	14.70	14.57	

Statistical analyses

Statistical analysis title	Analysis of CDAI ≤2.8 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-3.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.29
upper limit	0.94

Statistical analysis title	Analysis of CDAI ≤2.8 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.59
upper limit	1.48

Statistical analysis title	Analysis of CDAI ≤2.8 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.24
upper limit	5.47

Secondary: Percentage of Participants Achieving DAS28-4 (ESR) <2.6 at Month 6

End point title	Percentage of Participants Achieving DAS28-4 (ESR) <2.6 at Month 6

End point description:

DAS28-4 (ESR) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and ESR (mm/hour) using the following: DAS28-4(ESR) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*ln(ESR) + 0.014* PtGA (mm). Total score range: 0 to 9.4, higher score indicates higher disease activity. DAS28-4 (ESR) <2.6 indicates disease remission.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	353	344	346	
Units: Percentage of participants				
number (not applicable)	11.33	12.79	13.58	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (ESR) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.03
upper limit	2.93

Statistical analysis title	Analysis of DAS28-4 (ESR) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	690
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.11
upper limit	4.18

Statistical analysis title	Analysis of DAS28-4 (ESR) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.51
upper limit	2.47

Secondary: Percentage of Participants Achieving DAS28-4 (CRP) <2.6 at Month 6	
End point title	Percentage of Participants Achieving DAS28-4 (CRP) <2.6 at Month 6
End point description:	
DAS28-4 (CRP) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and CRP (mg/L) using the following: DAS28-4(CRP) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP+1) + 0.014* PtGA (mm) + 0.96. Total score range: 0 to 9.4, higher score indicates higher disease activity. DAS28-4 (CRP) <2.6 indicates remission.	
End point type	Secondary
End point timeframe:	
Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	345	348	
Units: Percentage of participants				
number (not applicable)	22.69	32.75	30.17	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (CRP) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-9.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.68
upper limit	-3.3

Statistical analysis title	Analysis of DAS28-4 (CRP) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	2.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.86
upper limit	9.07

Statistical analysis title	Analysis of DAS28-4 (CRP) <2.6 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in remission rate
Point estimate	-6.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.94
upper limit	-0.83

Secondary: Percentage of Participants Achieving SDAI ≤11 at Month 6

End point title	Percentage of Participants Achieving SDAI ≤11 at Month 6

End point description:

SDAI is the numerical sum of five outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity), and CRP (mg/dL). SDAI total score ranges from 0 to 86. SDAI ≤3.3 indicates disease remission, >3.4 to 11 indicates low disease activity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	345	348	
Units: Percentage of participants				
number (not applicable)	46.78	53.33	51.15	

Statistical analyses

Statistical analysis title	Analysis of SDAI ≤11 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.32
upper limit	0.84

Statistical analysis title	Analysis of SDAI ≤11 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.51
upper limit	9.68

Statistical analysis title	Analysis of SDAI ≤11 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-3.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.69
upper limit	3.37

Secondary: Percentage of Participants Achieving CDAI ≤10 at Month 6

End point title	Percentage of Participants Achieving CDAI ≤10 at Month 6

End point description:

CDAI is the numerical sum of four outcome parameters: TJC and SJC both based on a 28-joint assessment, PtGA and PGA both assessed on a 0 to 10 cm VAS (higher scores indicate greater affection due to disease activity). CDAI total score ranges from 0 to 76. CDAI ≤2.8 indicates disease remission, >2.8 to 10 indicates low disease activity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	358	347	350	
Units: Percentage of participants				
number (not applicable)	45.53	52.45	50.00	

Statistical analyses

Statistical analysis title	Analysis of CDAI ≤10 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.29
upper limit	0.85

Statistical analysis title	Analysis of CDAI ≤10 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.79
upper limit	9.39

Statistical analysis title	Analysis of CDAI ≤10 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-3.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.94
upper limit	3.09

Secondary: Percentage of Participants Achieving DAS28-4 (ESR) ≤3.2 at Month 6

End point title	Percentage of Participants Achieving DAS28-4 (ESR) ≤3.2 at Month 6

End point description:

DAS28-4 (ESR) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and ESR (mm/hour) using the following: DAS28-4(ESR) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*ln(ESR) + 0.014* PtGA (mm). Total score range: 0 to 9.4, higher score indicates higher disease activity. DAS28-4 (ESR) ≤3.2 indicates low disease activity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	353	344	346	
Units: Percentage of participants				
number (not applicable)	22.10	28.49	29.77	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (ESR) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.05
upper limit	0

Statistical analysis title	Analysis of DAS28-4 (ESR) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.9
upper limit	-0.87

Statistical analysis title	Analysis of DAS28-4 (ESR) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	690
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.17
upper limit	5.44

Secondary: Percentage of Participants Achieving DAS28-4 (CRP) ≤3.2 at Month 6	
End point title	Percentage of Participants Achieving DAS28-4 (CRP) ≤3.2 at Month 6
End point description:	
DAS28-4 (CRP) was calculated from the SJC and TJC (both based on a 28-joint assessment), PtGA (assessed on a 0 to 10 cm VAS; higher scores indicate greater affection due to disease activity) and CRP (mg/L) using the following: DAS28-4(CRP) = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP+1) + 0.014* PtGA + 0.96. Total score range: 0 to 9.4, higher score indicated higher disease activity. DAS28-4 (CRP) ≤3.2 indicates low disease activity.	
End point type	Secondary
End point timeframe:	
Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	345	348	
Units: Percentage of participants				
number (not applicable)	44.54	49.57	50.86	

Statistical analyses

Statistical analysis title	Analysis of DAS28-4 (CRP) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	702
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-4.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.92
upper limit	2.18

Statistical analysis title	Analysis of DAS28-4 (CRP) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-5.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.49
upper limit	1.52

Statistical analysis title	Analysis of DAS28-4 (CRP) ≤3.2 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in rresponse rate
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	6.47

Secondary: Percentage of Participants Achieving American College of Rheumatology Criteria 20% Improvement (ACR20) Response at Month 6

End point title	Percentage of Participants Achieving American College of Rheumatology Criteria 20% Improvement (ACR20) Response at Month 6

End point description:

ACR20 response is a ≥20% improvement in TJC or SJC and 20% improvement in 3 of the following 5 criteria: 1) PGA of disease activity, 2) PtGA of disease activity, 3) participant's assessment of pain, 4)

participant's assessment of functional disability via a health assessment questionnaire, and 5) CRP at each visit.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	354	345	349	
Units: Percentage of participants				
number (not applicable)	70.06	79.13	77.65	

Statistical analyses

Statistical analysis title	Analysis of ACR20 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-8.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.84
upper limit	-1.75

Statistical analysis title	Analysis of ACR20 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	694
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.22
upper limit	8.52

Statistical analysis title	Analysis of ACR20 at Month 6

Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	703
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.72
upper limit	0.44

Secondary: Percentage of Participants Achieving American College of Rheumatology Criteria 70% Improvement (ACR70) Response at Month 6

End point title	Percentage of Participants Achieving American College of Rheumatology Criteria 70% Improvement (ACR70) Response at Month 6

End point description:

ACR70 response is a ≥70% improvement in TJC or SJC and 70% improvement in 3 of the following 5 criteria: 1) PGA of disease activity, 2) PtGA of disease activity, 3) participant's assessment of pain, 4) participant's assessment of functional disability via a health assessment questionnaire, and 5) CRP at each visit.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	343	349	
Units: Percentage of participants				
number (not applicable)	19.66	27.11	22.64	

Statistical analyses

Statistical analysis title	Analysis of ACR70 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-6.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.61
upper limit	-0.93

Statistical analysis title	Analysis of ACR70 at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	4.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	10.23

Statistical analysis title	Analysis of ACR70 at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.09
upper limit	3.1

Secondary: Change From Baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI) at Month 6

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

End point description:

The HAQ-DI is a participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dressing and grooming, arising, eating, walking, reach, grip, hygiene and other activities over the past week. Each activity category consists of 2 to 3 items. Each item is scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Any activity requiring assistance from another individual or the use of an assistive device adjusts to a minimum score of 2 to represent a more limited functional status. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	348	350	
Units: Units on a scale				
least squares mean (standard error)	-0.52 (± 0.031)	-0.58 (± 0.031)	-0.54 (± 0.031)	

Statistical analyses

Statistical analysis title	Analysis of HAQ-DI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.011
upper limit	0.148

Statistical analysis title	Analysis of HAQ-DI at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.054
upper limit	0.105

Statistical analysis title	Analysis of HAQ-DI at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.122
upper limit	0.037

Secondary: Percentage of Participants Achieving an HAQ-DI Decrease of at Least 0.22 at Month 6

End point title	Percentage of Participants Achieving an HAQ-DI Decrease of at Least 0.22 at Month 6

End point description:

The HAQ-DI is a participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dressing and grooming, arising, eating, walking, reach, grip, hygiene and other activities over the past week. Each activity category consists of 2 to 3 items. Each item is scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Any activity requiring assistance from another individual or the use of an assistive device adjusts to a minimum score of 2 to represent a more limited functional status. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. A decrease of 0.22 or more is considered a positive response.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	348	350	
Units: Percentage of participants				
number (not applicable)	71.07	75.57	72.86	

Statistical analyses

Statistical analysis title	Analysis of HAQ-DI 0.22 Decrease at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-4.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.68
upper limit	2.55

Statistical analysis title	Analysis of HAQ-DI 0.22 Decrease at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.87
upper limit	5.44

Statistical analysis title	Analysis of HAQ-DI 0.22 Decrease at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in response rate
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.72
upper limit	9.43

Secondary: Change From Baseline in the Short-Form-36 (SF-36) Health Survey, Physical Component Score at Month 6

End point title	Change From Baseline in the Short-Form-36 (SF-36) Health Survey, Physical Component Score at Month 6

End point description:

The SF-36 health survey 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 health domains are aggregated into two summary scores known as the physical component summary (PCS) score and the mental component summary (MCS) score. Normalized domain scores, PCS and MCS scores are used in the analyses. The component and domain scores were scored using the United States (US) 1998 general population norms. The resulting norm-based T scores for both the SF-36 version 2 (v2) and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher PCS score represents better physical health status.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	355	346	349	
Units: Units on a scale				
least squares mean (standard error)	6.7 (± 0.44)	7.9 (± 0.43)	7.8 (± 0.43)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 PCS at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.28
upper limit	-0.11

Statistical analysis title	Analysis of SF-36 PCS at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	0.01

Statistical analysis title	Analysis of SF-36 PCS at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	1.2

Secondary: Change From Baseline in the SF-36 Health Survey, Mental Component Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Mental Component Score at Month 6

End point description:

The SF-36 health survey 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 health domains are aggregated into two summary scores known as the PCS score and the MCS score. Normalized domain scores, PCS and MCS scores are used in the analyses. The component and domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher MCS score represents better physical health status.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	355	346	349	
Units: Units on a scale				
least squares mean (standard error)	5.2 (± 0.52)	5.7 (± 0.51)	4.4 (± 0.51)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 MCS at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	0.85

Statistical analysis title	Analysis of SF-36 MCS at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	2.11

Statistical analysis title	Analysis of SF-36 MCS at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	2.56

Secondary: Change From Baseline in the SF-36 Health Survey, Physical Functioning Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Physical Functioning Domain Score at Month 6

End point description:

SF-36v2 acute is a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. The 10 items of the physical functioning scale represent levels and kinds of limitations between extremes of physical activities, including lifting and carrying groceries; climbing stairs; bending, kneeling, or stooping; walking moderate distances; self-care limitations. The physical functioning items capture the presence and extent of physical limitations using a 3-level response continuum. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher physical functioning domain score represents better physical functioning.

End point type	Secondary
End point timeframe: Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	348	349	
Units: Units on a scale				
least squares mean (standard error)	6.4 (± 0.52)	7.3 (± 0.52)	7.3 (± 0.52)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Physical Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	0.39

Statistical analysis title	Analysis of SF-36 Physical Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	0.42

Statistical analysis title	Analysis of SF-36 Physical Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	1.34

Secondary: Change From Baseline in the SF-36 Health Survey, Role Physical Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Role Physical Domain Score at Month 6

End point description:

SF-36v2 acute is a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and 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; and d) accomplishing less. Items in the role physical scale are answered on a 5-point scale. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher role physical domain score represents better role physical functioning.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	347	350	
Units: Units on a scale				
least squares mean (standard error)	6.7 (± 0.47)	7.0 (± 0.47)	6.3 (± 0.47)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Role Physical at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	703
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	0.87

Statistical analysis title	Analysis of SF-36 Role Physical at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.58

Statistical analysis title	Analysis of SF-36 Role Physical at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	1.91

Secondary: Change From Baseline in the SF-36 Health Survey, Bodily Pain Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Bodily Pain Domain Score at Month 6

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 bodily pain scale comprises of 2 items pertaining to the intensity of bodily pain and extent of interference with normal work activities. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher bodily pain domain score represents less bodily pain.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	348	350	
Units: Units on a scale				
least squares mean (standard error)	8.2 (± 0.48)	10.3 (± 0.48)	9.9 (± 0.48)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Bodily Pain at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.25
upper limit	-0.8

Statistical analysis title	Analysis of SF-36 Bodily Pain at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	-0.47

Statistical analysis title	Analysis of SF-36 Bodily Pain at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	1.55

Secondary: Change From Baseline in the SF-36 Health Survey, General Health Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, General Health Domain Score at Month 6

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 general health scale consists of 5 items including a rating of health and 4 items addressing the respondent's view and expectations of his or her health. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher general health domain score represents better general health perceptions.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	347	350	
Units: Units on a scale				
least squares mean (standard error)	5.1 (± 0.44)	6.3 (± 0.44)	5.4 (± 0.44)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 General Health at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.27
upper limit	-0.05

Statistical analysis title	Analysis of SF-36 General Health at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.82

Statistical analysis title	Analysis of SF-36 General Health at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	1.98

Secondary: Change From Baseline in the SF-36 Health Survey, Vitality Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Vitality Domain Score at Month 6

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. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher vitality domain score represents better vitality.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	348	350	
Units: Units on a scale				
least squares mean (standard error)	5.6 (± 0.48)	6.1 (± 0.47)	5.7 (± 0.47)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Vitality at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.71
upper limit	0.68

Statistical analysis title	Analysis of SF-36 Vitality at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	1.05

Statistical analysis title	Analysis of SF-36 Vitality at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	1.57

Secondary: Change From Baseline in the SF-36 Health Survey, Social Functioning Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Social Functioning Domain Score at Month 6

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 2-item social functioning scale assesses health-related effects on quantity and quality of social activities. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher social functioning domain score represents better social functioning.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	348	350	
Units: Units on a scale				
least squares mean (standard error)	6.3 (± 0.52)	7.2 (± 0.52)	6.2 (± 0.52)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Social Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.45

Statistical analysis title	Analysis of SF-36 Social Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	1.51

Statistical analysis title	Analysis of SF-36 Social Functioning at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	2.39

Secondary: Change From Baseline in the SF-36 Health Survey, Role Emotional Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Role Emotional Domain Score at Month 6

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 3-item role emotional scale assesses 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. All 3 items are answered on a 5-point scale. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher role emotional domain score represents better role emotional functioning.

End point type	Secondary

End point timeframe:
Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	347	350	
Units: Units on a scale				
least squares mean (standard error)	6.7 (± 0.58)	7.7 (± 0.58)	6.0 (± 0.58)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Role Emotional at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	703
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	0.39

Statistical analysis title	Analysis of SF-36 Role Emotional at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.24

Statistical analysis title	Analysis of SF-36 Role Emotional at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX

Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	2.16

Secondary: Change From Baseline in the SF-36 Health Survey, Mental Health Domain Score at Month 6

End point title	Change From Baseline in the SF-36 Health Survey, Mental Health Domain Score at Month 6

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 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. All items are answered on a 5-point scale. The domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 v2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. A higher mental health domain score represents better mental health functioning.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	348	350	
Units: Units on a scale				
least squares mean (standard error)	5.3 (± 0.52)	5.5 (± 0.52)	5.0 (± 0.52)	

Statistical analyses

Statistical analysis title	Analysis of SF-36 Mental Health at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	1.08

Statistical analysis title	Analysis of SF-36 Mental Health at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	1.86

Statistical analysis title	Analysis of SF-36 Mental Health at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	1.62

Secondary: Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire at Month 6

End point title	Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire at Month 6

End point description:

The WPAI: Rheumatoid Arthritis is a 6 item questionnaire that is specific for rheumatoid arthritis and yields four types of scores: absenteeism, presenteeism (impairment at work/reduced job effectiveness), work productivity loss and activity impairment. WPAI outcomes are expressed as impairment percentages ranging from 0 to 100, with higher numbers indicating greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	341	343	
Units: Percentage of impairment				
least squares mean (standard error)				
Work hours missed due to problems	-2.62 (± 0.717)	-2.19 (± 0.700)	-1.75 (± 0.741)	
Work hours missed other reason	0.14 (± 1.019)	0.43 (± 0.991)	-0.77 (± 1.059)	
Hours worked in past 7 days	4.13 (± 1.729)	-0.82 (± 1.672)	1.28 (± 1.788)	
Problems affecting productivity	-1.94 (± 0.228)	-2.14 (± 0.224)	-1.95 (± 0.232)	
Problem affecting daily activities	-2.24 (± 0.137)	-2.47 (± 0.138)	-2.24 (± 0.139)	
% work time missed due to health	-4.51 (± 1.790)	-3.41 (± 1.794)	-1.87 (± 1.831)	
% impairment while working due to health	-19.38 (± 2.276)	-21.44 (± 2.235)	-19.52 (± 2.320)	
% overall work impairment due to health	-20.16 (± 2.663)	-22.27 (± 2.638)	-21.87 (± 2.710)	
% activity impairment due to health	-22.36 (± 1.375)	-24.74 (± 1.383)	-22.45 (± 1.394)	

Statistical analyses

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed due to problems	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.279
upper limit	1.427

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed due to problems	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX

Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.783
upper limit	1.044

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed due to problems	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.349
upper limit	1.462

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed other reason	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.928
upper limit	2.346

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed other reason	

Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.832
upper limit	3.64

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Work hours missed other reason	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	3.911

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Hours worked in past 7 days	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	4.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	9.37

Statistical analysis title	Analysis of WAPI at Month 6

Statistical analysis description: Hours worked in past 7 days	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.736
upper limit	7.43

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Hours worked in past 7 days	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.65
upper limit	2.454

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problems affecting productivity	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.373
upper limit	0.786

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problems affecting productivity	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.578
upper limit	0.607

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problems affecting productivity	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.784
upper limit	0.4

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problem affecting daily activities	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.112
upper limit	0.587

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problem affecting daily activities	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.341
upper limit	0.357

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: Problem affecting daily activities	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.582
upper limit	0.122

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % work time missed due to health	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.748
upper limit	3.553

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % work time missed due to health	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.339
upper limit	2.067

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % work time missed due to health	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.283
upper limit	3.207

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % impairment while working due to health	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.726
upper limit	7.858

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description:	
% impairment while working due to health	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.777
upper limit	6.068

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description:	
% impairment while working due to health	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.839
upper limit	3.998

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description:	
% overall work impairment due to health	

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.664
upper limit	8.877

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % overall work impairment due to health	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.164
upper limit	8.58

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % overall work impairment due to health	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.307
upper limit	6.51

Statistical analysis title	Analysis of WAPI at Month 6

Statistical analysis description: % activity impairment due to health	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.118
upper limit	5.873

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % activity impairment due to health	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.411
upper limit	3.573

Statistical analysis title	Analysis of WAPI at Month 6
Statistical analysis description: % activity impairment due to health	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.818
upper limit	1.225

Secondary: Change From Baseline in the EuroQol European Quality of Life-5 Dimensions (EuroQol EQ-5D) at Month 6

End point title	Change From Baseline in the EuroQol European Quality of Life-5 Dimensions (EuroQol EQ-5D) at Month 6

End point description:

The EQ-5D is a participant rated questionnaire to assess health-related quality of life in terms of a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression; 1 indicates better health state (no problems); 3 indicates worst health state ("confined to bed"). Scoring formula developed by EuroQol Group assigns a utility value for each domain in the profile. Score is transformed and results in a total score range -0.594 to 1.000; higher score indicates a better health state.

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	348	351	
Units: Units on a scale				
least squares mean (standard error)				
Utility score	0.20 (± 0.013)	0.22 (± 0.013)	0.22 (± 0.013)	
Mobility score	-0.29 (± 0.027)	-0.26 (± 0.027)	-0.28 (± 0.027)	
Self-care score	-0.27 (± 0.028)	-0.33 (± 0.028)	-0.32 (± 0.028)	
Usual activities score	-0.24 (± 0.029)	-0.26 (± 0.029)	-0.30 (± 0.029)	
Pain/discomfort score	-0.32 (± 0.026)	-0.34 (± 0.026)	-0.37 (± 0.026)	
Anxiety/depression score	-0.21 (± 0.029)	-0.24 (± 0.029)	-0.22 (± 0.029)	
VAS score	20.84 (± 1.100)	20.98 (± 1.100)	19.61 (± 1.100)	

Statistical analyses

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6

Statistical analysis description:

Utility score

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.057
upper limit	0.011

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Utility score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.054
upper limit	0.013

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Utility score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.031
upper limit	0.036

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Mobility score	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX

Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.098
upper limit	0.042

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Mobility score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.079
upper limit	0.06

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Mobility score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.089

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Self-care score	

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.014
upper limit	0.127

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Self-care score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.027
upper limit	0.114

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Self-care score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.083
upper limit	0.058

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6

Statistical analysis description: Usual activities score	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.062
upper limit	0.084

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Usual activities score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.129

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Usual activities score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.029
upper limit	0.118

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Pain/discomfort score	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.041
upper limit	0.091

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Pain/discomfort score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.015
upper limit	0.116

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Pain/discomfort score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.041
upper limit	0.091

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Anxiety/depression score	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.046
upper limit	0.103

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Anxiety/depression score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.066
upper limit	0.083

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: Anxiety/depression score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.094
upper limit	0.055

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: VAS score	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.934
upper limit	2.648

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: VAS score	
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.556
upper limit	4.016

Statistical analysis title	Analysis of EuroQol EQ-5D at Month 6
Statistical analysis description: VAS score	
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX

Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.425
upper limit	4.171

Secondary: Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale Total Score at Month 6

End point title	Change From Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale Total Score at Month 6

End point description:

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

End point type	Secondary

End point timeframe:

Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 5 mg BID + MTX	Adalimumab 40 mg + MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	348	352	
Units: Units on a scale				
least squares mean (standard error)	7.14 (± 0.500)	7.59 (± 0.498)	6.07 (± 0.499)	

Statistical analyses

Statistical analysis title	Analysis of FACIT-F at Month 6
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 5 mg BID + MTX
Number of subjects included in analysis	705
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	-0.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.706
upper limit	0.808

Statistical analysis title	Analysis of FACIT-F at Month 6
Comparison groups	Tofacitinib 5 mg BID v Adalimumab 40 mg + MTX
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.178
upper limit	2.325

Statistical analysis title	Analysis of FACIT-F at Month 6
Comparison groups	Tofacitinib 5 mg BID + MTX v Adalimumab 40 mg + MTX
Number of subjects included in analysis	700
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS mean difference
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.266
upper limit	2.779

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were assessed from informed consent up to at least 28 calendar days after last dose of investigational product. AEs were recorded from the time the subject has taken at least one dose of study treatment through last subject visit.

Adverse event reporting additional description:

An event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 participant and non-serious in another participant, or 1 participant may have experienced both a serious and non-serious event.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

One active tofacitinib 5 mg tablet orally BID plus placebo MTX (prior dose) orally every week plus placebo adalimumab 40 mg subcutaneously (SC) every other week for up to 12 months.

Reporting group title	Adalimumab 40 mg + MTX

Reporting group description:

One placebo tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus active adalimumab 40 mg SC every other week for up to 12 months.

Reporting group title	Tofacitinib 5 mg BID + MTX

Reporting group description:

One active tofacitinib 5 mg tablet orally BID plus active MTX (prior dose) orally every week plus placebo adalimumab 40 mg SC every other week for up to 12 months.

Serious adverse events	Tofacitinib 5 mg BID	Adalimumab 40 mg + MTX	Tofacitinib 5 mg BID + MTX
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 384 (9.11%)	24 / 386 (6.22%)	27 / 376 (7.18%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	2	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Enteropathy-associated T-cell lymphoma			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobular breast carcinoma in situ			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Meningioma			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pregnancy			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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	2 / 384 (0.52%)	1 / 386 (0.26%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 384 (0.00%)	2 / 386 (0.52%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Acute respiratory failure			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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	1 / 384 (0.26%)	1 / 386 (0.26%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 384 (0.26%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid lung			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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			
Exposure via father			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Fibula fracture			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Hip fracture			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	3 / 376 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			

subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Rib fracture			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Tibia fracture			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Cor pulmonale			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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 ischaemia			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Wolff-Parkinson-White syndrome			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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			
Cerebellar infarction			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertonia			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Hypoaesthesia			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radicular syndrome			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Syncope			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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			
Pancytopenia			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Corneal thinning			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Necrotising retinitis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Diverticulum intestinal			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Intestinal obstruction			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Vomiting			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			

subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	2 / 384 (0.52%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Hepatitis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Diabetic nephropathy			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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 colic			
subjects affected / exposed	0 / 384 (0.00%)	2 / 386 (0.52%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bone disorder			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Osteochondrosis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Rheumatoid arthritis			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Bacteraemia			

subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	3 / 384 (0.78%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial sepsis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis tuberculous			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	2 / 376 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingo-oophoritis			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 384 (0.00%)	1 / 386 (0.26%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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
Cellulitis with abscess			
subjects affected / exposed	0 / 384 (0.00%)	0 / 386 (0.00%)	1 / 376 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 384 (0.26%)	0 / 386 (0.00%)	0 / 376 (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: 5 %

Non-serious adverse events	Tofacitinib 5 mg BID	Adalimumab 40 mg + MTX	Tofacitinib 5 mg BID + MTX
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 384 (13.28%)	69 / 386 (17.88%)	72 / 376 (19.15%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 384 (2.08%)	26 / 386 (6.74%)	23 / 376 (6.12%)
occurrences (all)	8	38	28
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 384 (5.73%)	18 / 386 (4.66%)	16 / 376 (4.26%)
occurrences (all)	28	23	19
Upper respiratory tract infection			
subjects affected / exposed	25 / 384 (6.51%)	29 / 386 (7.51%)	37 / 376 (9.84%)
occurrences (all)	35	37	48

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported