Clinical trial results:
An Exploratory Phase 2, Randomized, Double-blind, Multicenter Study To Assess The Effects Of Tofacitinib (CP-690,550) ON Magnetic Resonance Imaging Endpoints, In Methotrexate Naïve Subjects With Early Active Rheumatoid Arthritis

Summary

EudraCT number	2010-020890-18
Trial protocol	CZ HU
Global end of trial date	05 November 2013

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	A3921068

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01164579
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 Clinical Trials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer Clinical Trials.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 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the effect of CP-690,550 administered as a Disease-Modifying Antirheumatic Drug (DMARD) monotherapy or in combination with Methotrexate (MTX) vs MTX alone on changes from baseline in wrist and metacarpophalangeal joints (MCP) bone marrow edema at Month 6 and wrist and MCP synovitis at Month 3, as assessed by utilizing the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) in subjects with early Rheumatoid Arthritis (RA).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Chile: 11
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Mexico: 35
Country: Number of subjects enrolled	Puerto Rico: 3
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	109
EEA total number of subjects	42

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)	98
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study was initiated on 25 October 2010 and completed on 05 November 2013. Subjects were enrolled from 9 countries (Poland, Chile, Croatia, Czech Republic, Hungary, Argentina, Mexico, Puerto Rico and United States).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)

Arm description:

Subjects received CP-690,550 tablets, twice daily (BID), and MTX capsules, for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	CP-690,550
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 milligram (mg) tablets, orally (PO), twice daily (BID) for a maximum of 12 months.

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

Dosage and administration details:

10 mg per week (mg/week) to 20 mg/week, PO for a maximum of 12 months. MTX dose was titrated as follows: 10 mg once weekly for 4 weeks; if well tolerated, then at Month 1 titrated up to 15 mg once weekly for 4 weeks; if well tolerated, then at Month 2 titrated up to 20 mg once weekly for the duration of the study. A single dose reduction of MTX 5 mg was allowed because of lack of tolerance, as long as the subject remained on a dose of at least MTX 10 mg weekly.

Arm title	Tofacitinib (CP- 690,550)

Arm description:

Subjects received CP-690,550 tablets, BID and matching placebo MTX capsules for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Arm type	Experimental

Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	CP-690,550
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg tablets, PO, BID for a maximum of 12 months.

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

Dosage and administration details:

Matching placebo MTX capsules, PO, once weekly for a maximum of 12 months. To maintain the blind, matching placebo MTX was titrated as follows: 4 capsules once weekly for 4 weeks; if well tolerated, at Month 1 titrated up to 6 capsules once weekly for 4 weeks; if well tolerated, then at Month 2 titrated up to 8 capsules once weekly for the duration of the study. A single dose reduction of MTX placebo to 2 capsules was allowed because of lack of tolerance, as long as the subject remained on a dose of at least 4 MTX placebo capsules weekly.

Arm title	Methotrexate

Arm description:

Subjects received MTX capsules and matching placebo CP-690,550 tablets. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg/week to 20 mg/week, PO. MTX dose was titrated as follows: 10 mg once weekly for 4 weeks; if well tolerated, then at Month 1 titrated up to 15 mg once weekly for 4 weeks; if well tolerated, then at Month 2 titrated up to 20 mg once weekly for the duration of the study. A single dose reduction of MTX 5 mg was allowed because of lack of tolerance, as long as the subject remained on a dose of at least MTX 10 mg weekly.

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

Dosage and administration details:

Matching placebo CP-690,550 tablets, PO, BID.

Number of subjects in period 1	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate
Started	36	36	37
Completed	28	27	21
Not completed	8	9	16
Consent withdrawn by subject	2	5	3
Adverse Event	4	2	5

Protocol Violation	-	1	2
Lost to follow-up	1	1	-
Reason not Specified	1	-	-
Lack of efficacy	-	-	6

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Reporting group description:	
Subjects received CP-690,550 tablets, twice daily (BID), and MTX capsules, for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	
Reporting group title	Tofacitinib (CP- 690,550)
Reporting group description:	
Subjects received CP-690,550 tablets, BID and matching placebo MTX capsules for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	
Reporting group title	Methotrexate
Reporting group description:	
Subjects received MTX capsules and matching placebo CP-690,550 tablets. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	

Reporting group values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate
Number of subjects	36	36	37
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 47.8 ± 12.3	 50.8 ± 12.8	 47.8 ± 11.6
Gender categorical Units: Subjects			
Female	31	30	29
Male	5	6	8

Reporting group values	Total		
Number of subjects	109		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	90		
Male	19		

End points

End points reporting groups

Reporting group title	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Reporting group description:	
Subjects received CP-690,550 tablets, twice daily (BID), and MTX capsules, for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	
Reporting group title	Tofacitinib (CP- 690,550)
Reporting group description:	
Subjects received CP-690,550 tablets, BID and matching placebo MTX capsules for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	
Reporting group title	Methotrexate
Reporting group description:	
Subjects received MTX capsules and matching placebo CP-690,550 tablets. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.	

Primary: Change From Baseline to Month 3 in Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) Wrist and Metacarpophalangeal (MCP) Synovitis

End point title	Change From Baseline to Month 3 in Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) Wrist and Metacarpophalangeal (MCP) Synovitis
End point description:	
Synovitis: an area in synovial compartment that shows above normal postgadolinium enhancement of thickness greater than width of normal synovium. T1-weighted images were acquired before,after administration of intravenous (IV) contrast agent containing gadolinium. IV contrast was required to demonstrate enhancing synovitis. Synovitis was scored 0 to 3 in 3 wrist regions in each of the first through fifth MCP joints. Score of 0 is normal,with no enhancement or enhancement up to thickness of normal synovium,while scores of 1 to 3(mild, moderate, severe) refer to increments of one-third of presumed maximum volume of enhancing tissue in synovial compartment. Total synovitis score ranges from a minimum of 0 to a maximum of 24. A negative value in synovitis change from baseline score indicates improvement. Evaluable Set: all randomized subjects who received at least 1 dose of randomized investigational drug and for whom a variable is nonmissing at both baseline and the specified time point.	
End point type	Primary
End point timeframe:	
Month 3	

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	32	31	
Units: score on a scale				
least squares mean (standard error)	-0.8 (± 0.41)	-0.69 (± 0.4)	-0.17 (± 0.4)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2696 [1]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in least squares (LS) Mean
Point estimate	-0.63
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.58
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[1] - 2-sided p-value; alpha equals (=) 0.10.

Statistical analysis title	Tofacitinib vs MTX
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550)
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3561 [2]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Mean
Point estimate	-0.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.46
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[2] - 2-sided p-value; alpha=0.10.

Primary: Change From Baseline to Month 6 in OMERACT RAMRIS Wrist and MCP Bone Marrow Edema

End point title	Change From Baseline to Month 6 in OMERACT RAMRIS Wrist and MCP Bone Marrow Edema

End point description:

Bone edema was assessed at 25 anatomic locations: 15 in 1 wrist and 10 in attached hand. Bone edema was defined as a lesion within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content. Each bone was scored separately; the scale was 0 to 3 based on the proportion of bone with edema, as follows 0: no edema; 1: 1-33 per cent (%) of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. OMERACT RAMRIS total bone edema score for hands/wrists was sum of the individual scores for each location. Thus the maximum score per hand/wrist was 75 (range 0-75). Increasing score=greater severity. Evaluable Set.

End point type	Primary

End point timeframe:

Month 6

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	29	28	
Units: score on a scale				
least squares mean (standard error)	-1.26 (± 0.41)	-1.45 (± 0.42)	0.29 (± 0.42)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0089 [3]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.52
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.59

Notes:

[3] - 2-sided p-value; alpha= 0.10.

Statistical analysis title	Tofacitinib vs MTX
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0038 [4]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.72
upper limit	-0.76
Variability estimate	Standard error of the mean
Dispersion value	0.59

Notes:

[4] - 2-sided p-value; alpha= 0.10.

Secondary: Change From Baseline to Months 1, 6, and 12 in OMERACT RAMRIS Wrist and MCP Synovitis

End point title	Change From Baseline to Months 1, 6, and 12 in OMERACT RAMRIS Wrist and MCP Synovitis

End point description:

Synovitis is defined as an area in the synovial compartment that shows above normal postgadolinium enhancement of a thickness greater than the width of the normal synovium. T1-weighted images were acquired before and after the administration of intravenous contrast agent containing gadolinium. Intravenous contrast was required to demonstrate enhancing synovitis. Synovitis was scored 0 to 3 in 3 wrist regions and in each of the first through fifth MCP joints. A score of 0 is normal, with no enhancement or enhancement up to the thickness of normal synovium, while scores of 1 to 3 (mild, moderate, severe) refer to increments of one-third of the presumed maximum volume of enhancing tissue in the synovial compartment. Total synovitis score ranges from a minimum of 0 to a maximum of 24. A negative value in synovitis change from Baseline score indicates an improvement. Evaluable Set.

End point type	Secondary

End point timeframe:

Month 1, 6, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	31	35	
Units: score on a scale				
least squares mean (standard error)				
Month 1 (n=28,31,35)	-0.42 (± 0.42)	-0.34 (± 0.4)	-0.17 (± 0.38)	
Month 6 (n=33,29,28)	-1.22 (± 0.4)	-1.29 (± 0.41)	-0.28 (± 0.42)	
Month 12 (n=29,26,21)	-2.26 (± 0.41)	-1.16 (± 0.43)	-0.66 (± 0.46)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6576 [5]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.19
upper limit	0.69
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[5] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7565 [6]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.09
upper limit	0.74
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[6] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1038 [7]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.94

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.89
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[7] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0868 [8]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.98
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.59

Notes:

[8] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0103 [9]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.62
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[9] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.435 [10]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.53
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.63

Notes:

[10] - 2-sided p-value; alpha=0.10.

Secondary: Change From Baseline to Months 1, 3, and 12 in OMERACT RAMRIS Bone Marrow Edema in Wrist and MCP

End point title	Change From Baseline to Months 1, 3, and 12 in OMERACT RAMRIS Bone Marrow Edema in Wrist and MCP

End point description:

Bone edema was assessed at 25 anatomic locations: 15 in 1 wrist and 10 in attached hand. Bone edema was defined as a lesion within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content. Each bone was scored separately; the scale was 0 to 3 based on the proportion of bone with edema, as follows 0: no edema; 1: 1-33% of bone edematous; 2: 34-66% of bone edematous; 3: 67-100%. OMERACT RAMRIS total bone edema score for hands/wrists was sum of the individual scores for each location. Thus the maximum score per hand/wrist was 75 (range 0-75). Increasing score=greater severity. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 3, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	32	35	
Units: score on a scale				
least squares mean (standard error)				
Month 1 (n=28,31,35)	-0.29 (± 0.43)	0.19 (± 0.41)	0.11 (± 0.39)	
Month 3 (n=30,32,31)	-0.77 (± 0.42)	-0.86 (± 0.41)	0.47 (± 0.41)	
Month 12 (n=29,26,21)	-1.52 (± 0.42)	-1.7 (± 0.43)	0.59 (± 0.46)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.489 [11]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.36
upper limit	0.56
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[11] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8817 [12]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.85
upper limit	1.02
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[12] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0351 [13]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.24

Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.21
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.59

Notes:

[13] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0231 [14]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.32
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.28
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[14] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008 [15]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.13
upper limit	-1.08
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[15] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003 [16]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-2.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.32
upper limit	-1.25
Variability estimate	Standard error of the mean
Dispersion value	0.63

Notes:

[16] - 2-sided p-value; alpha=0.10.

Secondary: Change From Baseline to Months 1, 3, 6, and 12 in OMERACT RAMRIS Wrist and MCP Erosions

End point title	Change From Baseline to Months 1, 3, 6, and 12 in OMERACT RAMRIS Wrist and MCP Erosions

End point description:

Bone erosion assessed at 25 anatomic locations: 15 in 1 wrist and 10 in attached hand. Each site was scored in 1.0 increments from 0 (no damage) to 10 (severe damage), indicating erosion (each unit=10% bone loss) of original articular bone. OMERACT RAMRIS total erosion score for hands/wrists was sum of the individual scores for each location. Thus the maximum score per hand/wrist is 250 (range 0-250). Increasing score=greater severity. Evaluable Set.

End point type	Secondary

End point timeframe:

Month 1, 3, 6, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	32	35	
Units: score on a scale				
least squares mean (standard error)				
Month 1 (n=28,31,35)	-0.12 (± 0.25)	0.27 (± 0.25)	0.27 (± 0.24)	
Month 3 (n=30,32,31)	-0.12 (± 0.25)	0.36 (± 0.24)	0.44 (± 0.25)	
Month 6 (n=33,29,28)	-0.06 (± 0.25)	-0.02 (± 0.25)	0.65 (± 0.25)	
Month 12 (n=29,26,21)	-0.11 (± 0.25)	-0.08 (± 0.25)	1.18 (± 0.26)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2689 [17]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.96
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[17] - 2-sided p-value; alpha=0.10 .

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550)
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9935 [18]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.58
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[18] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1086 [19]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.57

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.15
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[19] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8092 [20]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.66
upper limit	0.49
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[20] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0463 [21]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.29
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[21] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0624 [22]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.25
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[22] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [23]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.9
upper limit	-0.69
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:

[23] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008 [24]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.26

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.87
upper limit	-0.65
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:

[24] - 2-sided p-value; alpha=0.10.

Secondary: Modified Total Sharp Score (mTSS) at Months 6 and 12

End point title	Modified Total Sharp Score (mTSS) at Months 6 and 12

End point description:

Modified TSS is a measure of change in joint health. TSS is defined as joint space narrowing score (range 0 [no narrowing] to 168 [high narrowing]) plus (+) erosion score (range is from 0 [no erosion] to 280 [high erosion]). The modified TSS range is from 0 (no damage) to 448 (bad joint status). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 6, 12.

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: score on a scale				
least squares mean (standard error)				
Month 6 (n=29,27,28)	11.28 (± 0.5)	10.7 (± 0.51)	11.77 (± 0.52)	
Month 12 (n=26,25,22)	11.7 (± 0.51)	10.69 (± 0.52)	12.21 (± 0.54)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5019 [25]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.48

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.68
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[25] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550)
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1462 [26]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.28
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[26] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.49 [27]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.74
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.74

Notes:

[27] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0459
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.76
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.75

Secondary: Change From Baseline to Months 6 and 12 in mTSS

End point title	Change From Baseline to Months 6 and 12 in mTSS

End point description:

Modified TSS is a measure of change in joint health. TSS is defined as joint space narrowing score (range 0 [no narrowing] to 168 [high narrowing]) + erosion score (range is from 0 [no erosion] to 280 [high erosion]). The modified TSS range is from 0 (no damage) to 448 (bad joint status). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 6, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	28	
Units: scores on a scale				
least squares mean (standard error)				
Month 6 (n=29,27,28)	0.44 (± 0.5)	-0.14 (± 0.51)	0.93 (± 0.52)	
Month 12 (n=26,25,22)	0.85 (± 0.51)	-0.15 (± 0.52)	1.36 (± 0.54)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5019 [28]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.68
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[28] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1462 [29]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.28
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[29] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.49 [30]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.74
upper limit	0.72

Variability estimate	Standard error of the mean
Dispersion value	0.74

Notes:

[30] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0459 [31]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.76
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.75

Notes:

[31] - 2-sided p-value; alpha=0.10.

Secondary: Joint Space Narrowing (JSN) Scores at Months 6 and 12

End point title	Joint Space Narrowing (JSN) Scores at Months 6 and 12

End point description:

JSN score (a component of the modified TSS) is a measure of change in joint health. JSN score range is 0 (no narrowing) to 168 (high narrowing). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 6, 12.

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	28	
Units: score on a scale				
least squares mean (standard error)				
Month 6 (n=29,27,28)	5.45 (± 0.34)	5.11 (± 0.35)	5.52 (± 0.36)	
Month 12 (n=26,25,22)	5.59 (± 0.35)	5.05 (± 0.36)	5.88 (± 0.37)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8959 [32]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.89
upper limit	0.76
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[32] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4193 [33]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.25
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[33] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5764 [34]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.29

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.13
upper limit	0.56
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[34] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1101 [35]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.69
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[35] - 2-sided p-value; alpha=0.10.

Secondary: Change From Baseline to Months 6 and 12 in JSN Scores

End point title	Change From Baseline to Months 6 and 12 in JSN Scores

End point description:

JSN score (a component of the modified TSS) is a measure of change in joint health. JSN score range is 0 (no narrowing) to 168 (high narrowing). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Months 6 and 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	28	
Units: scores on a scale				
least squares mean (standard error)				

Month 6 (n=29,27,28)	0.29 (± 0.34)	-0.06 (± 0.35)	0.35 (± 0.36)	
Month 12 (n=26,25,22)	0.43 (± 0.35)	-0.12 (± 0.36)	0.71 (± 0.37)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8959 [36]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.89
upper limit	0.76
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[36] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4193 [37]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.25
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[37] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5764 [38]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.13
upper limit	0.56
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[38] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1101 [39]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.69
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[39] - 2-sided p-value; alpha=0.10.

Secondary: Erosion Scores at Months 6 and 12

End point title	Erosion Scores at Months 6 and 12

End point description:

Erosion score (a component of the modified TSS) is a measure of change in joint health. Erosion score range is from 0 (no erosion) to 280 (high erosion). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Months 6, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	28	
Units: scores on a scale				
least squares mean (standard error)				
Month 6 (n=29,27,28)	5.84 (± 0.24)	5.59 (± 0.25)	6.26 (± 0.25)	
Month 12 (n=26,25,22)	6.1 (± 0.25)	5.64 (± 0.26)	6.33 (± 0.27)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2351 [40]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[40] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0631 [41]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.27
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:
[41] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5369 [42]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.83
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:
[42] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.062 [43]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.31
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:
[43] - 2-sided p-value; alpha=0.10.

Secondary: Change From Baseline to Months 6 and 12 in Erosion Score

End point title	Change From Baseline to Months 6 and 12 in Erosion Score

End point description:

Erosion score (a component of the modified TSS) is a measure of change in joint health. Erosion score range is from 0 (no erosion) to 280 (high erosion). Increase from baseline represents disease progression and / or joint worsening; no change represents halting of disease progression; a decrease represents improvement. Evaluable Set; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:
Months 6, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	27	28	
Units: scores on a scale				
least squares mean (standard error)				
Month 6 (n=29,27,28)	0.16 (± 0.24)	-0.1 (± 0.25)	0.58 (± 0.25)	
Month 12 (n=26,25,22)	0.42 (± 0.25)	-0.05 (± 0.26)	0.65 (± 0.27)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2351 [44]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:
[44] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0631 [45]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.27
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[45] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5369 [46]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.83
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[46] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.062 [47]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.31
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:

[47] - 2-sided p-value; alpha=0.10.

Secondary: Percentage of Subjects With an American College of Rheumatology

(ACR) 20 Percent (%) Improvement (ACR20) Response

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 20 Percent (%) Improvement (ACR20) Response

End point description:

ACR20 response: greater than or equal to (>=) 20% improvement in tender joint count; >=20% improvement in swollen joint count; and >=20% improvement in at least 3 of 5 remaining ACR core measures: Subject's Assessment of Pain; Subject's Global Assessment of Disease Activity; Physician Global Assessment of Disease Activity; self-assessed disability (disability index of the Health Assessment Questionnaire[HAQ]);and C-Reactive Protein (CRP). FAS Non-Responder Imputation (NRI) method: subjects with missing values were considered to be non-responders. n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=35,35,37)	42.86	57.14	29.73	
Month 2 (n=35,36,37)	68.57	61.11	40.54	
Month 3 (n=35,36,37)	77.14	61.11	48.65	
Month 6 (n=35,36,37)	74.29	66.67	45.95	
Month 9 (n=35,36,37)	71.43	58.33	43.24	
Month 12 (n=35,36,37)	71.43	61.11	43.24	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.243
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	13.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.36
upper limit	31.62
Variability estimate	Standard error of the mean
Dispersion value	11.24

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0147
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	27.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.91
upper limit	45.9
Variability estimate	Standard error of the mean
Dispersion value	11.24

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0127
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.51
upper limit	46.54
Variability estimate	Standard error of the mean
Dispersion value	11.25

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0724
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	20.57
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.73
upper limit	39.41
Variability estimate	Standard error of the mean
Dispersion value	11.45

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0086
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.63
upper limit	46.35
Variability estimate	Standard error of the mean
Dispersion value	10.85

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2808
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	12.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.54
upper limit	31.47

Variability estimate	Standard error of the mean
Dispersion value	11.55

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0102
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.19
upper limit	46.48
Variability estimate	Standard error of the mean
Dispersion value	11.03

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0679
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	20.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.04
upper limit	39.39
Variability estimate	Standard error of the mean
Dispersion value	11.35

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0115
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.81
upper limit	46.55
Variability estimate	Standard error of the mean
Dispersion value	11.16

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1921
Method	Normal approximation to the binomial
Parameter estimate	Median difference (final values)
Point estimate	15.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.94
upper limit	34.12
Variability estimate	Standard error of the mean
Dispersion value	11.56

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0115
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.81
upper limit	46.55

Variability estimate	Standard error of the mean
Dispersion value	11.16

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1203
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	17.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.05
upper limit	36.79
Variability estimate	Standard error of the mean
Dispersion value	11.5

Secondary: Percentage of Subjects With an ACR 50% Improvement (ACR50) Response

End point title	Percentage of Subjects With an ACR 50% Improvement (ACR50) Response

End point description:

ACR50 response: >=50% improvement in tender or swollen joint counts and 50% improvement in 3 of the following 5 criteria: 1) Physician's Global Assessment of Disease Activity, 2) Subject's Assessment of disease activity, 3) Subject's Assessment of Pain, 4) Subject's assessment of functional disability via a HAQ, and 5) CRP at each visit. FAS NRI; n=number of subjects assess for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=35,35,37)	22.86	22.86	2.7	
Month 2 (n=35,36,37)	45.71	33.33	16.22	
Month 3 (n=35,36,37)	48.57	50	24.32	
Month 6 (n=35,36,37)	57.14	47.22	21.62	

Month 9 (n=35,36,37)	57.14	44.44	29.73	
Month 12 (n=35,36,37)	57.14	44.44	29.73	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0078
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	20.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	7.68
upper limit	32.62
Variability estimate	Standard error of the mean
Dispersion value	7.58

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0078
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	20.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	7.68
upper limit	32.62
Variability estimate	Standard error of the mean
Dispersion value	7.58

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0044
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	29.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	12.43
upper limit	46.56
Variability estimate	Standard error of the mean
Dispersion value	10.37

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0845
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	17.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.79
upper limit	33.43
Variability estimate	Standard error of the mean
Dispersion value	9.92

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0275
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	24.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.14
upper limit	42.35

Variability estimate	Standard error of the mean
Dispersion value	11

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0186
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	25.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	7.71
upper limit	43.63
Variability estimate	Standard error of the mean
Dispersion value	10.91

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0009
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	35.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	17.82
upper limit	53.22
Variability estimate	Standard error of the mean
Dispersion value	10.75

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0169
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	25.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	7.95
upper limit	43.24
Variability estimate	Standard error of the mean
Dispersion value	10.72

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0147
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	27.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.91
upper limit	45.9
Variability estimate	Standard error of the mean
Dispersion value	11.24

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1882
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.68
upper limit	33.11

Variability estimate	Standard error of the mean
Dispersion value	11.18

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0147
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	27.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.91
upper limit	45.9
Variability estimate	Standard error of the mean
Dispersion value	11.24

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1882
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.68
upper limit	33.11
Variability estimate	Standard error of the mean
Dispersion value	11.18

Secondary: Percentage of Subjects With an ACR 70% Improvement (ACR70) Response

End point title	Percentage of Subjects With an ACR 70% Improvement (ACR70) Response

End point description:

ACR70 response: >=70% improvement in tender or swollen joint counts and 70% improvement in 3 of the following 5 criteria: 1) Physician's Global Assessment of Disease Activity, 2) Subject's Assessment of

Disease Activity, 3) Subject's Assessment of Pain, 4) Subject's Assessment of Functional Disability via a HAQ, and 5) CRP at each visit. FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary
End point timeframe:	
Month 1, 2, 3, 6, 9, 12	

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=35,35,37)	8.57	2.86	0	
Month 2 (n=35,36,37)	31.43	22.22	5.41	
Month 3 (n=35,36,37)	25.71	27.78	10.81	
Month 6 (n=35,36,37)	34.29	30.56	21.62	
Month 9 (n=35,36,37)	31.43	33.33	18.92	
Month 12 (n=35,36,37)	22.86	33.33	21.62	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.07
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	8.57
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.78
upper limit	16.35
Variability estimate	Standard error of the mean
Dispersion value	4.73

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3102
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	2.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.77
upper limit	7.48
Variability estimate	Standard error of the mean
Dispersion value	2.81

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0027
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	26.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	11.73
upper limit	40.3
Variability estimate	Standard error of the mean
Dispersion value	8.68

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0324
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	16.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.88
upper limit	29.75

Variability estimate	Standard error of the mean
Dispersion value	7.86

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0969
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.13
upper limit	29.67
Variability estimate	Standard error of the mean
Dispersion value	8.97

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0606
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	16.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.09
upper limit	31.84
Variability estimate	Standard error of the mean
Dispersion value	9.04

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2276
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (net)
Point estimate	12.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	29.93
Variability estimate	Standard error of the mean
Dispersion value	10.49

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3827
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	8.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.9
upper limit	25.76
Variability estimate	Standard error of the mean
Dispersion value	10.23

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2177
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	12.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.18
upper limit	29.2

Variability estimate	Standard error of the mean
Dispersion value	10.15

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1558
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.29
upper limit	31.12
Variability estimate	Standard error of the mean
Dispersion value	10.15

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8997
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	1.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.89
upper limit	17.36
Variability estimate	Standard error of the mean
Dispersion value	9.8

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2587
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	11.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.34
upper limit	28.76
Variability estimate	Standard error of the mean
Dispersion value	10.36

Secondary: Disease Activity Score Based on 28-Joint Count and CRP (DAS28-3 [CRP])

End point title	Disease Activity Score Based on 28-Joint Count and CRP (DAS28-3 [CRP])

End point description:

DAS28-3 (CRP) was calculated from the swollen joint count and tender joint count using the 28 joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-3 (CRP) less than or equal to (<=) 3.2 implied low disease activity and greater than (>) 3.2 to 5.1 implied moderate to high disease activity, and DAS28-3 (CRP) less than (<) 2.6 = remission. FAS; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	36	37	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=36,36,37)	5.14 (± 0.96)	5.48 (± 0.78)	5.36 (± 0.8)	
Month 1 (n=33,35,37)	3.71 (± 1.15)	4.03 (± 0.91)	4.65 (± 1.07)	
Month 2 (n=33,33,32)	2.99 (± 1.17)	3.52 (± 1.15)	4.21 (± 1.31)	
Month 3 (n=33,33,31)	3.06 (± 1.02)	3.46 (± 1.09)	3.87 (± 1.43)	
Month 6 (n=31,29,29)	2.74 (± 1.15)	2.75 (± 0.95)	3.92 (± 1.49)	
Month 9 (n=30,28,24)	2.37 (± 0.98)	2.85 (± 0.9)	3.58 (± 1.63)	
Month 12 (n=27,26,20)	2.49 (± 1.02)	2.68 (± 1.05)	3.58 (± 1.4)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Baseline
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.56
upper limit	0.13

Statistical analysis title	Tofacitinib vs MTX at Baseline
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.19
upper limit	0.43

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.38
upper limit	-0.5

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.01
upper limit	-0.22

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.73
upper limit	-0.7

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.2
upper limit	-0.18

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.33
upper limit	-0.29

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.94
upper limit	0.12

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.75
upper limit	-0.61

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.73
upper limit	-0.63

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.81
upper limit	-0.61

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.73
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.33
upper limit	-0.13

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.69
upper limit	-0.51

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.51
upper limit	-0.29

Secondary: Change From Baseline in DAS28-3 (CRP)

End point title	Change From Baseline in DAS28-3 (CRP)

End point description:

DAS28-3 (CRP) was calculated from the swollen joint count and tender joint count using the 28 joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. FAS; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	37	
Units: scores on a scale				
least squares mean (standard error)				
Month 1 (n=33,35,37)	-1.61 (± 0.19)	-1.4 (± 0.18)	-0.73 (± 0.18)	
Month 2 (n=33,33,32)	-2.32 (± 0.19)	-1.88 (± 0.19)	-1.24 (± 0.19)	
Month 3 (n=33,33,31)	-2.25 (± 0.19)	-1.96 (± 0.19)	-1.57 (± 0.19)	

Month 6 (n=31,29,29)	-2.54 (± 0.19)	-2.55 (± 0.2)	-1.52 (± 0.19)	
Month 9 (n=30,28,24)	-2.92 (± 0.2)	-2.43 (± 0.2)	-1.76 (± 0.21)	
Month 12 (n=27,26,20)	-2.78 (± 0.2)	-2.61 (± 0.2)	-1.77 (± 0.22)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [48]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.88
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.31
upper limit	-0.45
Variability estimate	Standard error of the mean
Dispersion value	0.26

Notes:

[48] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0102 [49]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.1
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.26

Notes:

[49] - 2-sided p-value; alpha=0.10

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [50]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.52
upper limit	-0.64
Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:

[50] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0175 [51]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.08
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:

[51] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0125 [52]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.68
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.13
upper limit	-0.23

Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:
[52] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1457 [53]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.84
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:
[53] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003 [54]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.48
upper limit	-0.57
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:
[54] - 2-sided p-value; alpha=0.10

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002 [55]
Method	Difference in LS Means
Parameter estimate	Mean difference (final values)
Point estimate	-1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.49
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[55] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [56]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.63
upper limit	-0.69
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[56] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0196 [57]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.14
upper limit	-0.2

Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[57] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0007 [58]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.5
upper limit	-0.52
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[58] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0049 [59]
Method	mixed model repeated measures analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.32
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[59] - 2-sided p-value; alpha=0.10.

Secondary: Disease Activity Score Based on 28-Joint Count and Erythrocyte Sedimentation Rate (DAS28-4 [ESR])

End point title	Disease Activity Score Based on 28-Joint Count and Erythrocyte Sedimentation Rate (DAS28-4 [ESR])

End point description:

DAS28-4 (ESR) was calculated from swollen joint count and tender joint count using 28 joints count, ESR (millimeters per hour [mm/hour]) and Subject Global Assessment of disease activity (subject rated

arthritis activity assessment). Total score range: 0 to 9.4; higher score=more disease activity. DAS28-4 (ESR) =<3.2 implied low disease activity and >3.2 to 5.1 implied moderate to high disease activity, and DAS28-4 (ESR)
<2.6 = remission. FAS; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary
End point timeframe:	
Baseline, Month 1, 2, 3, 6, 9, 12	

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	36	37	
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=36,36,37)	6.25 (± 0.94)	6.5 (± 0.75)	6.44 (± 0.78)	
Month 1 (n=34,35,37)	4.6 (± 1.37)	4.93 (± 1.12)	5.51 (± 1.09)	
Month 2 (n=32,33,31)	3.77 (± 1.34)	4.36 (± 1.4)	5.05 (± 1.26)	
Month 3 (n=33,33,31)	3.66 (± 1.16)	4.12 (± 1.31)	4.63 (± 1.63)	
Month 6 (n=30,29,28)	3.32 (± 1.45)	3.51 (± 1.2)	4.75 (± 1.76)	
Month 9 (n=30,28,24)	3.06 (± 1.27)	3.58 (± 1.1)	4.17 (± 1.91)	
Month 12 (n=27,26,20)	3.02 (± 1.22)	3.47 (± 1.36)	4.13 (± 1.76)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Baseline
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.19
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.53
upper limit	0.15

Statistical analysis title	Tofacitinib vs MTX at Baseline
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.24
upper limit	0.36

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.91
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.4
upper limit	-0.42

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.01
upper limit	-0.14

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.28
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.82
upper limit	-0.73

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.25
upper limit	-0.13

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.55
upper limit	-0.38

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.12
upper limit	0.11

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.13
upper limit	-0.72

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.91
upper limit	-0.57

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.84
upper limit	-0.39

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	0.13

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.84
upper limit	-0.39

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.43
upper limit	0.11

Secondary: Change From Baseline in DAS28-4 (ESR)

End point title	Change From Baseline in DAS28-4 (ESR)

End point description:

DAS28-4 (ESR) was calculated from swollen joint count and tender joint count using 28 joints count, ESR (millimeters per hour [mm/hour]) and Subject Global Assessment of disease activity (subject rated arthritis activity assessment). Total score range: 0 to 9.4; higher score=more disease activity. FAS; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	35	37	
Units: scores on a scale				
least squares mean (standard error)				
Month 1 (n=34,35,37)	-1.77 (± 0.21)	-1.57 (± 0.21)	-0.94 (± 0.2)	
Month 2 (n=32,33,31)	-2.59 (± 0.22)	-2.08 (± 0.21)	-1.41 (± 0.21)	
Month 3 (n=33,33,31)	-2.69 (± 0.21)	-2.35 (± 0.21)	-1.8 (± 0.21)	
Month 6 (n=30,29,28)	-3.02 (± 0.22)	-2.81 (± 0.22)	-1.73 (± 0.22)	
Month 9 (n=30,28,24)	-3.29 (± 0.22)	-2.72 (± 0.22)	-2.14 (± 0.23)	
Month 12 (n=27,26,20)	-3.31 (± 0.22)	-2.84 (± 0.22)	-2.18 (± 0.24)	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0046 [60]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.32
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[60] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0303 [61]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.63
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.11
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[61] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001 [62]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.69
upper limit	-0.68

Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:
[62] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0255 [63]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.67
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.17
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:
[63] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0035 [64]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.39
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:
[64] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0683 [65]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.05
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[65] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [66]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.81
upper limit	-0.78
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[66] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0006 [67]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.59
upper limit	-0.56

Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[67] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0004 [68]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.67
upper limit	-0.62
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[68] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0706 [69]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.58
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.1
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[69] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008 [70]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-1.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.67
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[70] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0466 [71]
Method	mixed model repeated measures analysis
Parameter estimate	Difference in LS Means
Point estimate	-0.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.21
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[71] - 2-sided p-value; alpha=0.10.

Secondary: Percentage of Subjects With DAS28-3 (CRP) Response (Good or Moderate Improvement)

End point title	Percentage of Subjects With DAS28-3 (CRP) Response (Good or Moderate Improvement)

End point description:

DAS28-3(CRP) was calculated from the swollen joint count and tender joint count using 28-joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28 categorical responses define a good (absolute: <3.2 or >1.2 improvement from baseline [BL]), moderate (absolute: 3.2-5.1 or 0.6-1.2 change from BL), or no response (absolute: >5.1 or <0.6 change from BL). FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=33,35,37)	75.76	71.43	43.24	
Month 2 (n=34,36,37)	91.18	80.56	56.76	
Month 3 (n=34,36,37)	91.18	77.78	56.76	
Month 6 (n=34,36,37)	88.24	77.78	54.05	
Month 9 (n=34,36,37)	79.41	69.44	45.95	
Month 12 (n=34,36,37)	82.35	72.22	45.95	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0032 [72]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	32.51
Confidence interval	
level	90 %
sides	2-sided
lower limit	14.34
upper limit	50.68
Variability estimate	Standard error of the mean
Dispersion value	11.04

Notes:

[72] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0115 [73]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.18

Confidence interval	
level	90 %
sides	2-sided
lower limit	9.81
upper limit	46.55
Variability estimate	Standard error of the mean
Dispersion value	11.16

Notes:

[73] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002 [74]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	18.81
upper limit	50.02
Variability estimate	Standard error of the mean
Dispersion value	9.48

Notes:

[74] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0231 [75]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	23.79
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.55
upper limit	41.03
Variability estimate	Standard error of the mean
Dispersion value	10.48

Notes:

[75] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3

Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002 [76]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	18.81
upper limit	50.02
Variability estimate	Standard error of the mean
Dispersion value	9.48

Notes:

[76] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0493 [77]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	21.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.43
upper limit	38.61
Variability estimate	Standard error of the mean
Dispersion value	10.69

Notes:

[77] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [78]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.18

Confidence interval	
level	90 %
sides	2-sided
lower limit	17.92
upper limit	50.43
Variability estimate	Standard error of the mean
Dispersion value	9.88

Notes:

[78] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.027 [79]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	23.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	6.07
upper limit	41.37
Variability estimate	Standard error of the mean
Dispersion value	10.73

Notes:

[79] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0018 [80]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	15.8
upper limit	51.12
Variability estimate	Standard error of the mean
Dispersion value	10.73

Notes:

[80] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0363 [81]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	23.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.02
upper limit	41.96
Variability estimate	Standard error of the mean
Dispersion value	11.22

Notes:

[81] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [82]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	36.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	19.16
upper limit	53.64
Variability estimate	Standard error of the mean
Dispersion value	10.48

Notes:

[82] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0177 [83]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	26.27

Confidence interval	
level	90 %
sides	2-sided
lower limit	8.04
upper limit	44.5
Variability estimate	Standard error of the mean
Dispersion value	11.08

Notes:

[83] - 2-sided p-value; alpha=0.10.

Secondary: Percentage of Subjects With DAS28-3 (CRP) Score =<3.2

End point title	Percentage of Subjects With DAS28-3 (CRP) Score =<3.2

End point description:

DAS28-3(CRP) was calculated from the swollen joint count and tender joint count using 28-joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-3(CRP) =<3.2 implied low disease activity. FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=33,35,37)	33.33	17.14	10.81	
Month 2 (n=34,36,37)	50	36.11	21.62	
Month 3 (n=34,36,37)	50	41.67	21.62	
Month 6 (n=34,36,37)	61.76	55.56	27.03	
Month 9 (n=34,36,37)	64.71	58.33	29.33	
Month 12 (n=34,36,37)	61.76	50	27.03	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0197 [84]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	22.52

Confidence interval	
level	90 %
sides	2-sided
lower limit	6.62
upper limit	38.42
Variability estimate	Standard error of the mean
Dispersion value	9.66

Notes:

[84] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4379 [85]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	6.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.09
upper limit	19.76
Variability estimate	Standard error of the mean
Dispersion value	8.16

Notes:

[85] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0093 [86]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.4
upper limit	46.34
Variability estimate	Standard error of the mean
Dispersion value	10.92

Notes:

[86] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1669 [87]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.75
upper limit	31.73
Variability estimate	Standard error of the mean
Dispersion value	10.48

Notes:

[87] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0093 [88]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.4
upper limit	46.34
Variability estimate	Standard error of the mean
Dispersion value	10.92

Notes:

[88] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0596 [89]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	20.04

Confidence interval	
level	90 %
sides	2-sided
lower limit	2.53
upper limit	37.55
Variability estimate	Standard error of the mean
Dispersion value	10.64

Notes:
[89] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0017 [90]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.73
Confidence interval	
level	90 %
sides	2-sided
lower limit	16.51
upper limit	52.96
Variability estimate	Standard error of the mean
Dispersion value	11.07

Notes:
[90] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0097 [91]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.36
upper limit	46.69
Variability estimate	Standard error of the mean
Dispersion value	11.04

Notes:
[91] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9

Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0016 [92]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	16.68
upper limit	53.26
Variability estimate	Standard error of the mean
Dispersion value	11.11

Notes:

[92] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0102 [93]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	28.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	10.28
upper limit	46.91
Variability estimate	Standard error of the mean
Dispersion value	11.13

Notes:

[93] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0017 [94]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	34.73

Confidence interval	
level	90 %
sides	2-sided
lower limit	16.51
upper limit	52.96
Variability estimate	Standard error of the mean
Dispersion value	11.07

Notes:

[94] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0381 [95]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	22.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	4.74
upper limit	41.19
Variability estimate	Standard error of the mean
Dispersion value	11.07

Notes:

[95] - 2-sided p-value; alpha=0.10

Secondary: Percentage of Subjects With DAS28-3 (CRP) Score <2.6

End point title	Percentage of Subjects With DAS28-3 (CRP) Score <2.6

End point description:

DAS28-3(CRP) was calculated from the swollen joint count and tender joint count using 28-joints count and CRP (mg/L). Total score range: 0 to 9.4, higher score indicated more disease activity. DAS28-3(CRP) <2.6 implied remission. FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=33,35,37)	18.18	5.71	5.41	

Month 2 (n=34,36,37)	35.29	16.67	8.11	
Month 3 (n=34,36,37)	32.35	22.22	13.51	
Month 6 (n=34,36,37)	47.06	33.33	16.22	
Month 9 (n=34,36,37)	50	38.89	18.92	
Month 12 (n=34,36,37)	47.06	33.33	13.51	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0959 [96]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	12.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.15
upper limit	25.4
Variability estimate	Standard error of the mean
Dispersion value	7.67

Notes:

[96] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9544 [97]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.58
upper limit	9.19
Variability estimate	Standard error of the mean
Dispersion value	5.4

Notes:

[97] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2

Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0036 [98]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	27.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	11.81
upper limit	42.55
Variability estimate	Standard error of the mean
Dispersion value	9.34

Notes:

[98] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.264 [99]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	8.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.04
upper limit	21.16
Variability estimate	Standard error of the mean
Dispersion value	7.66

Notes:

[99] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0544 [100]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	18.83

Confidence interval	
level	90 %
sides	2-sided
lower limit	2.72
upper limit	34.95
Variability estimate	Standard error of the mean
Dispersion value	9.79

Notes:

[100] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.329 [101]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	8.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.96
upper limit	23.38
Variability estimate	Standard error of the mean
Dispersion value	8.92

Notes:

[101] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0032 [102]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	30.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	13.59
upper limit	48.09
Variability estimate	Standard error of the mean
Dispersion value	10.48

Notes:

[102] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6

Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0845 [103]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	17.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.79
upper limit	33.43
Variability estimate	Standard error of the mean
Dispersion value	9.92

Notes:

[103] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0037 [104]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	31.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	13.44
upper limit	48.72
Variability estimate	Standard error of the mean
Dispersion value	10.72

Notes:

[104] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.054 [105]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	19.96

Confidence interval	
level	90 %
sides	2-sided
lower limit	2.91
upper limit	37.02
Variability estimate	Standard error of the mean
Dispersion value	10.36

Notes:

[105] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [106]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.54
Confidence interval	
level	90 %
sides	2-sided
lower limit	16.7
upper limit	50.39
Variability estimate	Standard error of the mean
Dispersion value	10.24

Notes:

[106] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0401 [107]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	19.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.92
upper limit	35.71
Variability estimate	Standard error of the mean
Dispersion value	9.66

Notes:

[107] - 2-sided p-value; alpha=0.10.

Secondary: Percentage of Subjects With DAS28-4 (ESR) Response (Good or

Moderate Improvement)	
End point title	Percentage of Subjects With DAS28-4 (ESR) Response (Good or Moderate Improvement)

End point description:

DAS28-4(ESR) was calculated from swollen joint count and tender joint count using 28 joints count, ESR (mm/hour) and Subject's Global Assessment of Disease Activity (subject rated arthritis activity assessment). Total score range: 0 to 9.4, higher score=more disease activity. DAS28 categorical responses define a good (absolute: <3.2 or >1.2 improvement from BL), moderate (absolute: 3.2-5.1 or 0.6-1.2 change from BL), or no response (absolute: >5.1 or <0.6 change from BL). FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	35	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=34,35,37)	67.65	62.86	29.73	
Month 2 (n=32,33,31)	85.29	69.44	59.46	
Month 3 (n=33,33,31)	91.18	69.44	51.35	
Month 6 (n=30,29,28)	85.29	77.78	51.35	
Month 9 (n=30,28,24)	82.35	72.22	45.95	
Month 12 (n=27,26,20)	79.41	69.44	45.95	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [108]
Method	[Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	37.91
Confidence interval	
level	90 %
sides	2-sided
lower limit	19.83
upper limit	55.99
Variability estimate	Standard error of the mean
Dispersion value	10.99

Notes:
[108] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0028 [109]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	14.87
upper limit	51.38
Variability estimate	Standard error of the mean
Dispersion value	11.09

Notes:
[109] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0105 [110]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	25.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	9.21
upper limit	42.45
Variability estimate	Standard error of the mean
Dispersion value	10.1

Notes:
[110] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.37 [111]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	9.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.33
upper limit	28.3
Variability estimate	Standard error of the mean
Dispersion value	11.13

Notes:

[111] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [112]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	39.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	24.11
upper limit	55.53
Variability estimate	Standard error of the mean
Dispersion value	9.54

Notes:

[112] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1076 [113]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	18.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.4
upper limit	36.59

Variability estimate	Standard error of the mean
Dispersion value	11.24

Notes:

[113] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008 [114]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	17.13
upper limit	50.75
Variability estimate	Standard error of the mean
Dispersion value	10.21

Notes:

[114] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0139 [115]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	26.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.74
upper limit	44.1
Variability estimate	Standard error of the mean
Dispersion value	10.74

Notes:

[115] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [116]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	36.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	19.16
upper limit	53.64
Variability estimate	Standard error of the mean
Dispersion value	10.48

Notes:
[116] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0177
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	26.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	8.04
upper limit	44.5
Variability estimate	Standard error of the mean
Dispersion value	11.08

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0018 [117]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	15.8
upper limit	51.12

Variability estimate	Standard error of the mean
Dispersion value	10.73

Notes:

[117] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0363 [118]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	23.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.02
upper limit	41.96
Variability estimate	Standard error of the mean
Dispersion value	11.22

Notes:

[118] - 2-sided p-value; alpha=0.10.

Secondary: Percentage of Subjects With DAS28-4 (ESR) <=3.2

End point title	Percentage of Subjects With DAS28-4 (ESR) <=3.2

End point description:

DAS28-4(ESR) was calculated from swollen joint count and tender joint count using 28 joints count, ESR (mm/hour) and Subject's Global Assessment of Disease Activity (subject rated arthritis activity assessment). Total score range: 0 to 9.4, higher score=more disease activity. DAS28-4(ESR) <=3.2 implied low disease activity. FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary

End point timeframe:

Month 1, 2, 3, 6, 9, 12

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=34,35,37)	20.59	8.57	2.7	
Month 2 (n=34,36,37)	35.29	13.89	8.11	
Month 3 (n=34,36,37)	32.35	30.56	13.51	
Month 6 (n=34,36,37)	41.18	27.78	18.92	
Month 9 (n=34,36,37)	44.12	33.33	18.92	

Month 12 (n=34,36,37)	50	30.56	16.22	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.016 [119]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	17.88
Confidence interval	
level	90 %
sides	2-sided
lower limit	5.66
upper limit	30.1
Variability estimate	Standard error of the mean
Dispersion value	7.42

Notes:

[119] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2798 [120]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	5.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.06
upper limit	14.8
Variability estimate	Standard error of the mean
Dispersion value	5.43

Notes:

[120] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0036 [121]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	27.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	11.81
upper limit	42.55
Variability estimate	Standard error of the mean
Dispersion value	9.34

Notes:

[121] - 2-sided p-value; alpha=0.10

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4287 [122]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	5.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.23
upper limit	17.79
Variability estimate	Standard error of the mean
Dispersion value	7.3

Notes:

[122] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0544 [123]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	18.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.72
upper limit	34.95

Variability estimate	Standard error of the mean
Dispersion value	9.79

Notes:
[123] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0732 [124]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	17.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.39
upper limit	32.69
Variability estimate	Standard error of the mean
Dispersion value	9.51

Notes:
[124] - 2-sided p-value; alpha=0.10

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.036 [125]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	22.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	4.79
upper limit	39.72
Variability estimate	Standard error of the mean
Dispersion value	10.61

Notes:
[125] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3688 [126]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	8.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.35
upper limit	25.07
Variability estimate	Standard error of the mean
Dispersion value	9.85

Notes:

[126] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0182 [127]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	25.19
Confidence interval	
level	90 %
sides	2-sided
lower limit	7.63
upper limit	42.76
Variability estimate	Standard error of the mean
Dispersion value	10.67

Notes:

[127] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1558 [128]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.29
upper limit	31.12

Variability estimate	Standard error of the mean
Dispersion value	10.15

Notes:

[128] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0012 [129]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	33.78
Confidence interval	
level	90 %
sides	2-sided
lower limit	16.51
upper limit	51.05
Variability estimate	Standard error of the mean
Dispersion value	10.49

Notes:

[129] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1426 [130]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (net)
Point estimate	14.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.74
upper limit	30.42
Variability estimate	Standard error of the mean
Dispersion value	9.78

Notes:

[130] - 2-sided p-value; alpha=0.10

Secondary: Percentage of Subjects With DAS28-4 (ESR) <2.6

End point title	Percentage of Subjects With DAS28-4 (ESR) <2.6

End point description:

DAS28-4(ESR) was calculated from swollen joint count and tender joint count using 28 joints count, ESR (mm/hour) and Subject's Global Assessment of Disease Activity (subject rated arthritis activity assessment). Total score range: 0 to 9.4, higher score=more disease activity. DAS28-4(ESR) <2.6 implied remission. FAS NRI; n=number of subjects assessed for the specified parameter at a given visit.

End point type	Secondary
End point timeframe: Month 1, 2, 3, 6, 9, 12	

End point values	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	36	37	
Units: percentage of subjects				
number (not applicable)				
Month 1 (n=34,35,37)	5.88	2.86	0	
Month 2 (n=34,36,37)	17.65	5.56	2.7	
Month 3 (n=34,36,37)	23.53	2.78	13.51	
Month 6 (n=34,36,37)	29.41	13.89	13.51	
Month 9 (n=34,36,37)	35.29	13.89	16.22	
Month 12 (n=34,36,37)	32.35	19.44	13.51	

Statistical analyses

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1449 [131]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	5.88
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.75
upper limit	12.52
Variability estimate	Standard error of the mean
Dispersion value	4.03

Notes:
[131] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 1
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3102 [132]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	2.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.77
upper limit	7.48
Variability estimate	Standard error of the mean
Dispersion value	2.81

Notes:

[132] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0342 [133]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	14.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.32
upper limit	26.55
Variability estimate	Standard error of the mean
Dispersion value	7.06

Notes:

[133] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 2
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.54 [134]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	2.85
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.8
upper limit	10.51

Variability estimate	Standard error of the mean
Dispersion value	4.65

Notes:

[134] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2759 [135]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	10.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.1
upper limit	25.13
Variability estimate	Standard error of the mean
Dispersion value	9.19

Notes:

[135] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 3
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0859 [136]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	-10.73
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.02
upper limit	-0.45
Variability estimate	Standard error of the mean
Dispersion value	6.25

Notes:

[136] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0985 [137]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	15.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.06
upper limit	31.73
Variability estimate	Standard error of the mean
Dispersion value	9.62

Notes:

[137] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 6
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9628 [138]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	0.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.86
upper limit	13.61
Variability estimate	Standard error of the mean
Dispersion value	8.05

Notes:

[138] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 9
Comparison groups	Methotrexate v Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0612 [139]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	19.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.31
upper limit	35.84

Variability estimate	Standard error of the mean
Dispersion value	10.19

Notes:
[139] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 9
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7807 [140]
Method	Normal approximation to
Parameter estimate	Mean difference (final values)
Point estimate	-2.32
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.08
upper limit	11.43
Variability estimate	Standard error of the mean
Dispersion value	8.36

Notes:
[140] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib Plus MTX vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX) v Methotrexate
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0544 [141]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	18.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.72
upper limit	34.95
Variability estimate	Standard error of the mean
Dispersion value	9.79

Notes:
[141] - 2-sided p-value; alpha=0.10.

Statistical analysis title	Tofacitinib vs MTX at Month 12
Comparison groups	Tofacitinib (CP- 690,550) v Methotrexate

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4937 [142]
Method	Normal approximation to the binomial
Parameter estimate	Mean difference (final values)
Point estimate	5.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	-8.32
upper limit	20.18
Variability estimate	Standard error of the mean
Dispersion value	8.66

Notes:

[142] - 2-sided p-value; alpha=0.10.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected up to 28 calendar days after the last administration of investigational product.

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as nonserious in another subject, or 1 subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Tofacitinib (CP- 690,550) Plus Methotrexate (MTX)

Reporting group description:

Subjects received CP-690,550 tablets, twice daily (BID), and MTX capsules, for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Reporting group title	Tofacitinib (CP- 690,550)

Reporting group description:

Subjects received CP-690,550 tablets, BID and matching placebo MTX capsules for a maximum of 12 months. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Reporting group title	Methotrexate

Reporting group description:

Subjects received MTX capsules and matching placebo CP-690,550 tablets. Subjects also received folate supplementation according to local MTX label guidelines and standard of care.

Serious adverse events	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	2 / 37 (5.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (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
Gastrointestinal disorders			
Haematochezia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
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			
Cholelithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Tofacitinib (CP-690,550) Plus Methotrexate (MTX)	Tofacitinib (CP-690,550)	Methotrexate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 36 (66.67%)	31 / 36 (86.11%)	29 / 37 (78.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 36 (2.78%)	6 / 36 (16.67%)	0 / 37 (0.00%)
occurrences (all)	1	6	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Local swelling			

subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Menorrhagia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Sexual dysfunction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Uterine fibrosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	1	3	0
Pharyngeal inflammation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 36 (16.67%)	0 / 36 (0.00%)	5 / 37 (13.51%)
occurrences (all)	7	0	8
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	3 / 37 (8.11%)
occurrences (all)	2	1	3
Blood bicarbonate decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 36 (2.78%)	3 / 36 (8.33%)	1 / 37 (2.70%)
occurrences (all)	1	4	1
Blood glucose increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	3
Haemoglobin decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	4	1	2
Liver function test abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Red blood cell count decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Weight increased			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Myocardial ischaemia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	2 / 37 (5.41%)
occurrences (all)	4	2	2
Hypoaesthesia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Tension headache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Lymph node pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Lymphadenopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			

subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Macrocytosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Neutrophilia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Thrombocytosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Scleritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Visual acuity reduced			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Xerophthalmia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	3	1	2
Abdominal tenderness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Dry mouth			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	2	1	1

Food poisoning			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Gastric disorder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 36 (0.00%)	5 / 36 (13.89%)	4 / 37 (10.81%)
occurrences (all)	0	6	4
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Hyperchlorhydria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Irritable bowel syndrome			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Stomatitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Hepatic steatosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Hypertransaminasaemia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	3	1	2
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	3 / 37 (8.11%)
occurrences (all)	3	0	3
Diffuse alopecia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	0 / 37 (0.00%)
occurrences (all)	1	4	0
Rosacea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	4	1	0
Back pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Joint swelling			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	5 / 37 (13.51%)
occurrences (all)	0	2	5
Rheumatoid nodule			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Tendonitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Anal abscess			

subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	3	0	0
Folliculitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Fungal skin infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	1	2	0
Nasopharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Oral fungal infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	2 / 37 (5.41%)
occurrences (all)	3	3	3
Pharyngotonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pneumonia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	2 / 37 (5.41%)
occurrences (all)	4	2	2
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	2	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Vulvovaginitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0

Hypertriglyceridaemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Hypoglycaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Increased appetite			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 September 2010	Bone marrow edema at 6 months was added as an additional primary endpoint.
15 December 2010	1. The definition of AEs was expanded to include signs and symptoms resulting from exposure during breast feeding. 2. The definition of hospitalization was expanded to include hospitalization for observation without a medical AE. 3. Potential cases of Drug-Induced Liver Injury (DILI) were added to the protocol.
22 August 2012	1. Reporting of laboratory abnormalities that warranted temporary discontinuation of study medication was added. 2. Treated infections were added. 3. Addition of a urine Human Chorionic Gonadotrophin (HCG) pregnancy test for female subjects of childbearing potential at each visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported