



## Clinical trial results:

### A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of Tofacitinib in Subjects with Active Ankylosing Spondylitis (AS)

#### Summary

EudraCT number	2011-005689-39
Trial protocol	HU CZ ES NL SK
Global end of trial date	18 March 2015

#### Results information

Result version number	v1 (current)
This version publication date	03 April 2016
First version publication date	03 April 2016

#### Trial information

##### Trial identification

Sponsor protocol code	A3921119
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01786668
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 March 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 March 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

This was a Phase 2, multicentre, randomised, double-blind, placebo-controlled dose ranging, parallel group efficacy and safety study designed to characterise the dose response of tofacitinib in participants with active AS.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki (World Medical Association 1996 and 2008) and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002). In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants. The final protocol and amendments were reviewed and approved by the Institutional Review Board(s) and/or Independent Ethics Committee(s) at each of the investigational centres participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	Hungary: 33
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Poland: 67
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 31
Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	207
EEA total number of subjects	128

Notes:

<b>Subjects enrolled per age group</b>	
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)	196
From 65 to 84 years	11
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A diagnosis of AS based on the Modified New York Criteria for AS (1984) with active disease defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of greater than or equal to ( $\geq$ ) 4 and back pain score (BASDAI Question 2) of  $\geq 4$  despite treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) (or intolerance to NSAIDs).

### 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	Investigator, Subject

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Tofacitinib 2 mg BID

Arm description:

Participants were administered 4 tablets (two 1 mg tablets of tofacitinib along with two 5 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.

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

Dosage and administration details:

Two 1 mg tablets of tofacitinib along with two 5 mg matching placebo tablets administered orally BID (in the AM and PM) for a total of 12 weeks.

<b>Arm title</b>	Tofacitinib 5 mg BID
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Arm description:

Participants were administered 4 tablets (one 5 mg tablet of tofacitinib, one 5 mg and two 1 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.

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

Dosage and administration details:

One 5 mg tablets of tofacitinib along with one 5 mg and two 1 mg matching placebo tablets administered orally BID (in the AM and PM) for a total of 12 weeks.

<b>Arm title</b>	Tofacitinib 10 mg BID
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Arm description:

Participants were administered 4 tablets (two 5 mg tablets of tofacitinib and two 1 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.

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

Dosage and administration details:

Two 5 mg tablets of tofacitinib along with two 1 mg matching placebo tablets administered orally BID (in the AM and PM) for a total of 12 weeks.

<b>Arm title</b>	Placebo BID
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Arm description:

Participants were administered 4 tablets (two 1 mg placebo tablets and two 5 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for tofacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two 1 mg matching placebo tablets along with two 5 mg matching placebo tablets administered orally BID (in the AM and PM) for a total of 12 weeks.

<b>Number of subjects in period 1</b>	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Started	52	52	52
Completed	51	51	47
Not completed	1	1	5
Consent withdrawn by subject	-	-	3
Adverse event, non-fatal	-	1	1
Pregnancy	-	-	-
Lost to follow-up	1	-	1

<b>Number of subjects in period 1</b>	Placebo BID
Started	51
Completed	47
Not completed	4
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Pregnancy	1
Lost to follow-up	-

## Baseline characteristics

### Reporting groups

Reporting group title	Tofacitinib 2 mg BID
Reporting group description: Participants were administered 4 tablets (two 1 mg tablets of tofacitinib along with two 5 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description: Participants were administered 4 tablets (one 5 mg tablet of tofacitinib, one 5 mg and two 1 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description: Participants were administered 4 tablets (two 5 mg tablets of tofacitinib and two 1 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Placebo BID
Reporting group description: Participants were administered 4 tablets (two 1 mg placebo tablets and two 5 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.	

Reporting group values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Number of subjects	52	52	52
Age categorical Units: Subjects			
Adults (18-64 years)	49	51	49
Elderly (from 65-84 years)	3	1	3
Age Continuous   Age Units: Years			
arithmetic mean	41.8	41.2	41.6
standard deviation	± 12.3	± 10.3	± 12.2
Gender, Male/Female Units: Participants			
Female	18	13	14
Male	34	39	38

Reporting group values	Placebo BID	Total	
Number of subjects	51	207	
Age categorical Units: Subjects			
Adults (18-64 years)	47	196	
Elderly (from 65-84 years)	4	11	
Age Continuous   Age Units: Years			
arithmetic mean	41.9	-	
standard deviation	± 12.9	-	
Gender, Male/Female Units: Participants			
Female	19	64	
Male	32	143	



## End points

### End points reporting groups

Reporting group title	Tofacitinib 2 mg BID
Reporting group description: Participants were administered 4 tablets (two 1 mg tablets of tofacitinib along with two 5 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description: Participants were administered 4 tablets (one 5 mg tablet of tofacitinib, one 5 mg and two 1 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description: Participants were administered 4 tablets (two 5 mg tablets of tofacitinib and two 1 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.	
Reporting group title	Placebo BID
Reporting group description: Participants were administered 4 tablets (two 1 mg placebo tablets and two 5 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.	

### Primary: Percentage of Participants Achieving 20 Percent (%) Improvement in Assessment of SpondyloArthritis International Society (ASAS) Score (ASAS 20) at Week 12

End point title	Percentage of Participants Achieving 20 Percent (%) Improvement in Assessment of SpondyloArthritis International Society (ASAS) Score (ASAS 20) at Week 12
End point description: The primary analysis of this outcome measure was performed using the Emax model. Clinical response to treatment was assessed according to ASAS20 criteria. ASAS20 responder had improvement of $\geq 20\%$ and $\geq 1$ unit in at least 3 domains (on a scale of 0 [least] to 10 [worst]) and no worsening of $\geq 20\%$ and less than or equal to ( $\leq$ ) 1 unit in the remaining domain. The domains are: Patient's Global Assessment of Disease Activity, spinal pain, function and inflammation (from BASDAI). Missing data were handled by nonresponsive (NRI)/ last observation carried forward (LOCF). Missing values due to a participant dropping out from the study were handled by setting the ASAS20 value to NRI. The LOCF approach was applied to missing components, if just some of the components of the ASAS20 were missing. Analysis population is the Full Analysis Set (FAS) which included all participants who were randomized to the study and received at least one dose of the randomized study drug (tofacitinib or placebo).	
End point type	Primary
End point timeframe: Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)	56	63	67.4	40.1



## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 12
Statistical analysis description: Emax model with 95% credible interval computed - 95% confidence interval below represents 95% credible interval.	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
Method	Emax Model
Parameter estimate	Risk difference (RD)
Point estimate	15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	30.3

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 12
Statistical analysis description: Emax model with 95% credible interval computed - 95% confidence interval below represents 95% credible interval.	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
Method	Emax Model
Parameter estimate	Risk difference (RD)
Point estimate	22.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.4
upper limit	37.7

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 12
Statistical analysis description: Emax model with 95% credible interval computed - 95% confidence interval below represents 95% credible interval.	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
Method	Emax Model
Parameter estimate	Risk difference (RD)
Point estimate	27.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	10.7
upper limit	43.4

### Primary: Percentage of Participants Achieving ASAS20 at Week 12

End point title	Percentage of Participants Achieving ASAS20 at Week 12
End point description:	
<p>The supportive analysis of this outcome measure was performed using the normal approximation for two proportions. Clinical response to treatment was assessed according to ASAS20 criteria. ASAS20 responder had improvement of <math>\geq 20\%</math> and <math>\geq 1</math> unit in at least 3 domains (on a scale of 0 [least] to 10 [worst]) and no worsening of <math>\geq 20\%</math> and <math>\leq 1</math> unit in the remaining domain. The domains are: Patient's Global Assessment of Disease Activity, spinal pain, function and inflammation (from BASDAI). Missing data were handled by NRI/LOCF. Missing values due to a participant dropping out from the study were handled by setting the ASAS20 value to NRI. The LOCF approach was applied to missing components, if just some of the components of the ASAS20 were missing. Analysis population is the FAS.</p>	
End point type	Primary
End point timeframe:	
Baseline, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)	51.92	80.77	55.77	41.18

### Statistical analyses

Statistical analysis title	Analysis of ASAS20 at Week 12
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.271
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	10.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.41
upper limit	29.9
Variability estimate	Standard error of the mean
Dispersion value	9.77

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 12
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	39.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.35
upper limit	56.83
Variability estimate	Standard error of the mean
Dispersion value	8.8

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 12
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.134
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	14.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	33.69
Variability estimate	Standard error of the mean
Dispersion value	9.74

## Secondary: Percentage of Participants Achieving 20% Improvement in ASAS Score at Weeks 2, 4 and 8

End point title	Percentage of Participants Achieving 20% Improvement in ASAS Score at Weeks 2, 4 and 8
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### End point description:

Clinical response to treatment was assessed according to ASAS20 criteria. ASAS20 responder had improvement of  $\geq 20\%$  and  $\geq 1$  unit in at least 3 domains (on a scale of 0 [least] to 10 [worst]) and no worsening of  $\geq 20\%$  and  $\leq 1$  unit in the remaining domain. The domains are: Patient's Global Assessment of Disease Activity, spinal pain, function and inflammation (from BASDAI). Missing data were handled by NRI/LOCF. Missing values due to a participant dropping out from the study were handled by setting the ASAS20 value to NRI. The LOCF approach was applied to missing components, if just some of the

components of the ASAS20 were missing. Analysis population is the FAS, n is the number of responders at each visit.

End point type	Secondary
End point timeframe:	
Baseline, Week 2, Week 4, Week 8	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=21,17,18,14)	40.38	32.69	34.62	27.45
Week 4 (n=25,29,25,17)	48.08	55.77	48.08	33.33
Week 8 (n=30, 37, 28, 22)	57.69	71.15	53.85	43.14

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.162
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	12.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	31.04
Variability estimate	Standard error of the mean
Dispersion value	9.24

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.561
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.44
upper limit	22.92
Variability estimate	Standard error of the mean
Dispersion value	9.02

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.43
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.65
upper limit	24.97
Variability estimate	Standard error of the mean
Dispersion value	9.09

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.123
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	14.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	33.5
Variability estimate	Standard error of the mean
Dispersion value	9.57

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.019
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.74
upper limit	41.13
Variability estimate	Standard error of the mean
Dispersion value	9.54

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.123
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	14.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	33.5
Variability estimate	Standard error of the mean
Dispersion value	9.57

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.135
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	14.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	33.66
Variability estimate	Standard error of the mean
Dispersion value	9.75

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	28.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.68
upper limit	46.36
Variability estimate	Standard error of the mean
Dispersion value	9.36

<b>Statistical analysis title</b>	Analysis of ASAS20 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.274
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	10.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.48
upper limit	29.9
Variability estimate	Standard error of the mean
Dispersion value	9.79

### Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Index of Disease Activity Score of the Sacroiliac (SI) Joints at Week 12

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) Index of Disease Activity Score of the Sacroiliac (SI) Joints at Week 12
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#### End point description:

SPARCC scoring consists of assessing six SI joint MRI image coronal slices representing the largest proportion of the synovial compartment of the SI joints for edema. The maximum score per slice was 2 and 12 for all 6 slices. The total maximum score for all SI joints across 6 slices is 72 and higher scores indicate more inflammation. A negative change from baseline indicates improvement. Missing data at Week 12 were imputed by LOCF if data at an early visit (discontinuation visit) were available. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
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#### End point timeframe:

Baseline, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	34
Units: Units on a scale				
least squares mean (standard error)	-1.7 (± 0.779)	-3.15 (± 0.788)	-3.55 (± 0.795)	-0.81 (± 0.806)

### Statistical analyses

Statistical analysis title	Analysis of SPARCC MRI (SI Joints) at Week 12
Comparison groups	Tofacitinib 2 mg BID v Placebo BID



Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.427
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.11
upper limit	1.32
Variability estimate	Standard error of the mean
Dispersion value	1.123

<b>Statistical analysis title</b>	Analysis of SPARCC MRI (SI Joints) at Week 12
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.039
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.58
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	1.13

<b>Statistical analysis title</b>	Analysis of SPARCC MRI (SI Joints) at Week 12
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.016
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.97
upper limit	-0.51

Variability estimate	Standard error of the mean
Dispersion value	1.131

## Secondary: Change from Baseline in SPARCC MRI Index of Disease Activity Score of the Spine at Week 12

End point title	Change from Baseline in SPARCC MRI Index of Disease Activity Score of the Spine at Week 12
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End point description:

SPARCC scoring of the MRI of the spine consists of assessing six disco-vertebral units (DVU) with 3 consecutive sagittal slices at each DVU. The maximum SPARCC score for all 6 DVUs is 108, with higher scores indicating more damage. A negative change from baseline indicates improvement. Missing data at Week 12 were imputed by LOCF if data at an early visit (discontinuation visit) were available. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	44	44	34
Units: Units on a scale				
least squares mean (standard error)	-3.09 (± 1.061)	-5.51 (± 1.063)	-6.57 (± 1.073)	-0.09 (± 1.085)

## Statistical analyses

Statistical analysis title	Analysis of SPARCC MRI (Spine) at Week 12
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.99
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	1.517

<b>Statistical analysis title</b>	Analysis of SPARCC MRI (Spine) at Week 12
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.42
upper limit	-2.42
Variability estimate	Standard error of the mean
Dispersion value	1.52

<b>Statistical analysis title</b>	Analysis of SPARCC MRI (Spine) at Week 12
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.48
upper limit	-3.46
Variability estimate	Standard error of the mean
Dispersion value	1.525

## **Secondary: Change from Baseline in Modified Berlin Ankylosing Spondylitis Spine Magnetic Resonance Imaging Activity Score (ASspiMRI) of the Spine at Week 12**

End point title	Change from Baseline in Modified Berlin Ankylosing Spondylitis Spine Magnetic Resonance Imaging Activity Score (ASspiMRI) of the Spine at Week 12
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### **End point description:**

Berlin modification of the ASspiMRI is a measure of acute lesion as determined by short-tau inversion recovery (STIR) sequences. All 23 DVU of the spine (from C2 to S1), defined as the region between 2 virtual lines through the middle of each vertebra, were scored in a single dimension, which is represented the highest level of inflammation in that particular DVU. Total spine ASspiMRI scores can range from 0-69 with higher scores indicating more disease activity. A negative change from baseline

indicates improvement. Missing data at Week 12 were imputed by LOCF if data at an early visit (discontinuation visit) were available. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	44	44	34
Units: Units on a scale				
least squares mean (standard error)	-1.05 ( $\pm$ 0.364)	-2.22 ( $\pm$ 0.364)	-2.13 ( $\pm$ 0.368)	-0.41 ( $\pm$ 0.372)

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASspiMRI of the Spine at Week 12
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.221
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.52

<b>Statistical analysis title</b>	Analysis of ASspiMRI of the Spine at Week 12
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.83
upper limit	-0.78
Variability estimate	Standard error of the mean
Dispersion value	0.52

<b>Statistical analysis title</b>	Analysis of ASspiMRI of the Spine at Week 12
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.75
upper limit	-0.68
Variability estimate	Standard error of the mean
Dispersion value	0.523

### Secondary: Percentage of Participants Achieving 40% Improvement in ASAS score at weeks 2, 4, 8 and 12

End point title	Percentage of Participants Achieving 40% Improvement in ASAS score at weeks 2, 4, 8 and 12
End point description:	
ASAS 40 is defined as $\geq 40\%$ and absolute change of $\geq 2$ units in at least 3 domains on a 0-10 scale (0=no disease activity, 10=high disease activity), and no worsening in the remaining domain. Missing data were handled by NRI/LOCF. Analysis population is the FAS, n is the number of responders at each visit.	
End point type	Secondary
End point timeframe:	
Baseline, Week 2, Week 4, Week 8, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=7, 7, 9, 8)	13.46	13.46	17.31	15.69

Week 4 (n=15, 17, 11, 8)	28.85	32.69	21.15	15.69
Week 8 (n=15, 18, 19, 14)	28.85	34.62	36.54	27.45
Week 12 (n=22, 24, 20, 10)	42.31	46.15	38.46	19.61

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.749
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	-2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.85
upper limit	11.4
Variability estimate	Standard error of the mean
Dispersion value	6.95

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.749
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	-2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.85
upper limit	11.4
Variability estimate	Standard error of the mean
Dispersion value	6.95

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.824
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.71
upper limit	15.95
Variability estimate	Standard error of the mean
Dispersion value	7.31

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.104
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	13.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.69
upper limit	29.01
Variability estimate	Standard error of the mean
Dispersion value	8.09

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.04
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	17.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	33.2
Variability estimate	Standard error of the mean
Dispersion value	8.26

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.473
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.46
upper limit	20.4
Variability estimate	Standard error of the mean
Dispersion value	7.62

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.875
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.4



Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.97
upper limit	18.76
Variability estimate	Standard error of the mean
Dispersion value	8.86

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.43
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.65
upper limit	24.97
Variability estimate	Standard error of the mean
Dispersion value	9.09

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.32
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	9.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.84
upper limit	27.01
Variability estimate	Standard error of the mean
Dispersion value	9.15

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.41
upper limit	39.99
Variability estimate	Standard error of the mean
Dispersion value	8.82

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	26.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.16
upper limit	43.93
Variability estimate	Standard error of the mean
Dispersion value	8.87

<b>Statistical analysis title</b>	Analysis of ASAS 40 at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.031
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	18.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.72
upper limit	35.99
Variability estimate	Standard error of the mean
Dispersion value	8.74

### Secondary: Percentage of Participants Achieving ASAS5/6 Response at Weeks 2, 4, 8 and 12

End point title	Percentage of Participants Achieving ASAS5/6 Response at Weeks 2, 4, 8 and 12
End point description:	
ASAS5/6 consists of 6 domains: the 4 used in ASAS20 (Patient's Global Assessment of Disease Activity, spinal pain, function, inflammation plus spinal mobility and an acute phase reactant, C Reactive Protein (CRP). ASAS 5/6 is defined as $\geq 20\%$ improvement in at least 5 domains and no worsening in the remaining domain. Missing data were handled by NRI/LOCF. Analysis population is the FAS, n is the number of responders at each visit.	
End point type	Secondary
End point timeframe:	
Baseline, Week 2, Week 4, Week 8, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=12, 7, 11, 4)	23.08	13.46	21.15	7.84
Week 4 (n=10, 16, 15, 4)	19.23	30.77	28.85	7.84
Week 8 (n=11, 22, 15, 5)	21.15	42.31	28.85	9.8
Week 12 (n=10, 26, 20, 8)	19.23	50	38.46	15.69

### Statistical analyses

Statistical analysis title	Analysis of ASAS5/6 Response at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.028
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	15.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.61
upper limit	28.86
Variability estimate	Standard error of the mean
Dispersion value	6.95

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.353
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	17.47
Variability estimate	Standard error of the mean
Dispersion value	6.05

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.05
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	13.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	26.64
Variability estimate	Standard error of the mean
Dispersion value	6.8

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.086
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	11.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	24.39
Variability estimate	Standard error of the mean
Dispersion value	6.64

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.37
upper limit	37.48
Variability estimate	Standard error of the mean
Dispersion value	7.43

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.65
upper limit	35.36
Variability estimate	Standard error of the mean
Dispersion value	7.32

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.106
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	11.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	25.13
Variability estimate	Standard error of the mean
Dispersion value	7.03

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	32.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.79
upper limit	48.22
Variability estimate	Standard error of the mean
Dispersion value	8.02

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	19.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.27
upper limit	33.81
Variability estimate	Standard error of the mean
Dispersion value	7.54

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.635
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	3.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	18.19
Variability estimate	Standard error of the mean
Dispersion value	7.47

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 8
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	34.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.45
upper limit	51.18
Variability estimate	Standard error of the mean
Dispersion value	8.6

<b>Statistical analysis title</b>	Analysis of ASAS5/6 Response at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.007
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.21
upper limit	39.34
Variability estimate	Standard error of the mean
Dispersion value	8.45



## Secondary: Change from Baseline of Ankylosing Spondylitis Disease Activity Score using C-Reactive Protein ASDAS(CRP) at Weeks 2, 4, 8 and 12

End point title	Change from Baseline of Ankylosing Spondylitis Disease Activity Score using C-Reactive Protein ASDAS(CRP) at Weeks 2, 4, 8 and 12
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End point description:

The ASDAS(CRP) is a derived score that uses back pain, duration of morning stiffness, Patient's Global Assessment of their disease and peripheral pain/swelling. The formula used for calculating the ASDAS(CRP) is  $0.12 \times \text{Back Pain} + 0.06 \times \text{Duration of Morning Stiffness} + 0.11 \times \text{Patient Global} + 0.07 \times \text{Peripheral Pain/Swelling} + 0.58 \times \ln(\text{CRP}+1)$ . The calculated score can be from 0 to no defined upper limit. A negative number indicates a reduction in the score which indicates decrease in disease activity. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	50
Units: Units on a scale				
least squares mean (standard error)				
Week 2	-0.68 ( $\pm$ 0.096)	-1 ( $\pm$ 0.096)	-0.97 ( $\pm$ 0.096)	-0.5 ( $\pm$ 0.097)
Week 4	-1.01 ( $\pm$ 0.099)	-1.2 ( $\pm$ 0.099)	-1.17 ( $\pm$ 0.099)	-0.58 ( $\pm$ 0.1)
Week 8	-1.08 ( $\pm$ 0.111)	-1.36 ( $\pm$ 0.111)	-1.32 ( $\pm$ 0.112)	-0.73 ( $\pm$ 0.112)
Week 12	-1.23 ( $\pm$ 0.119)	-1.41 ( $\pm$ 0.119)	-1.37 ( $\pm$ 0.121)	-0.68 ( $\pm$ 0.123)

## Statistical analyses

Statistical analysis title	Analysis of ASDAS(CRP) at Week 2
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Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
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Number of subjects included in analysis	101
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Analysis specification	Pre-specified
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Analysis type	
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P-value	= 0.175
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Method	Mixed models analysis
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Parameter estimate	Mean difference (final values)
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Point estimate	-0.19
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Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.136

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.136

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.136

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.141

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.34
Variability estimate	Standard error of the mean
Dispersion value	0.141

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.31
Variability estimate	Standard error of the mean
Dispersion value	0.141

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.158

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.63

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	-0.32
Variability estimate	Standard error of the mean
Dispersion value	0.157

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.159

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.171

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.171

<b>Statistical analysis title</b>	Analysis of ASDAS(CRP) at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.172

## Secondary: Percentage of Participants with ASDAS Clinically Important Improvement at Weeks 2, 4, 8 and 12

End point title	Percentage of Participants with ASDAS Clinically Important Improvement at Weeks 2, 4, 8 and 12
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End point description:

The ASDAS clinically important improvement was calculated from the ASDAS data. The ASDAS clinically important improvement is defined as change (decrease) from baseline of  $\geq 1.1$  units. Missing data were handled by NRI/LOCF. Analysis population is the FAS, n is the number of responders at each visit.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=14, 25, 21, 8)	26.92	48.08	40.38	15.69
Week4 (n=22, 30, 27, 10)	42.31	57.69	51.92	19.61
Week 8 (n=23, 31, 31, 15)	44.23	59.62	59.62	29.41
Week 12 (n=27, 33, 29, 14)	51.92	63.46	55.77	27.45

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 2
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Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
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Number of subjects included in analysis	103
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Analysis specification	Pre-specified
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Analysis type	
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P-value	= 0.159
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Method	Normal approximation for two proportions
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Parameter estimate	Risk difference (RD)
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Point estimate	11.24
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-4.41
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upper limit	26.89
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Variability estimate	Standard error of the mean
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Dispersion value	7.99
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<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 2
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Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 5 mg BID v Placebo BID
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Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	32.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.54
upper limit	49.24
Variability estimate	Standard error of the mean
Dispersion value	8.6

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	24.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.04
upper limit	41.36
Variability estimate	Standard error of the mean
Dispersion value	8.5

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.7



Confidence interval	
level	95 %
sides	2-sided
lower limit	5.41
upper limit	39.99
Variability estimate	Standard error of the mean
Dispersion value	8.82

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	38.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.79
upper limit	55.38
Variability estimate	Standard error of the mean
Dispersion value	8.82

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	32.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.9
upper limit	49.73
Variability estimate	Standard error of the mean
Dispersion value	8.88

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.114
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	14.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	33.22
Variability estimate	Standard error of the mean
Dispersion value	9.39

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	30.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.92
upper limit	48.49
Variability estimate	Standard error of the mean
Dispersion value	9.33

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	30.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.92
upper limit	48.49
Variability estimate	Standard error of the mean
Dispersion value	9.33

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.009
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	24.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.18
upper limit	42.76
Variability estimate	Standard error of the mean
Dispersion value	9.33

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	36.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	18.09
upper limit	53.94
Variability estimate	Standard error of the mean
Dispersion value	9.15

<b>Statistical analysis title</b>	Analysis of ASDAS Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	28.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.09
upper limit	46.55
Variability estimate	Standard error of the mean
Dispersion value	9.3

<b>Secondary: Percentage of Participants with ASDAS Major Improvement at Weeks 2, 4, 8 and 12</b>	
End point title	Percentage of Participants with ASDAS Major Improvement at Weeks 2, 4, 8 and 12
End point description: The ASDAS major improvement was calculated from the ASDAS data. The ASDAS major improvement was defined as change (decrease) from baseline of $\geq 2.0$ units. Missing data were handled by NRI/LOCF. Analysis population is the FAS, n is the number of responders at each visit.	
End point type	Secondary
End point timeframe: Baseline, Week 2, Week 4, Week 8, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=4, 4, 4, 1)	7.69	7.69	7.69	1.96
Week 4 (n=6, 6, 8, 3)	11.54	11.54	15.38	5.88
Week 8 (n=6, 14, 12, 5)	11.54	26.92	23.08	9.8
Week 12 (n=10, 12, 13, 6)	19.23	23.08	25	11.76

## Statistical analyses

Statistical analysis title	Analysis of ASDAS Major Improvement at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.17
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	13.91
Variability estimate	Standard error of the mean
Dispersion value	4.17

Statistical analysis title	Analysis of ASDAS Major Improvement at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.17
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	13.91
Variability estimate	Standard error of the mean
Dispersion value	4.17

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.17
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	13.91
Variability estimate	Standard error of the mean
Dispersion value	4.17

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.306
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	16.48
Variability estimate	Standard error of the mean
Dispersion value	5.52

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.306
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	16.48
Variability estimate	Standard error of the mean
Dispersion value	5.52

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.113
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	21.24
Variability estimate	Standard error of the mean
Dispersion value	5.99

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.775
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.18
upper limit	13.65
Variability estimate	Standard error of the mean
Dispersion value	6.08

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.021
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	17.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.56
upper limit	31.68
Variability estimate	Standard error of the mean
Dispersion value	7.43

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.064
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	13.27



Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	27.34
Variability estimate	Standard error of the mean
Dispersion value	7.17

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.292
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.42
upper limit	21.36
Variability estimate	Standard error of the mean
Dispersion value	7.09

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.125
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	11.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.16
upper limit	25.78
Variability estimate	Standard error of the mean
Dispersion value	7.38

<b>Statistical analysis title</b>	Analysis of ASDAS Major Improvement at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.078
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	13.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	27.96
Variability estimate	Standard error of the mean
Dispersion value	7.51

## Secondary: Percentage of Participants Achieving ASDAS Inactive Disease at Weeks 2, 4, 8 and 12

End point title	Percentage of Participants Achieving ASDAS Inactive Disease at Weeks 2, 4, 8 and 12
End point description: The ASDAS inactive disease was calculated from the ASDAS data. The ASDAS inactive disease was defined as ASDAS <1.3 units. Missing data were handled by NRI/LOCF. Analysis population is the FAS, n is the number of responders at each visit.	
End point type	Secondary
End point timeframe: Baseline, Week 2, Week 4, Week 8, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=1, 1, 1, 0)	1.92	1.92	1.92	0
Week 4 (n=1, 3, 4, 1)	1.92	5.77	7.69	1.96
Week 8 (n=3, 1, 5, 1)	5.77	1.92	9.62	1.96
Week 12 (n=7, 7, 8, 4)	13.46	13.46	15.38	7.84

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	5.66
Variability estimate	Standard error of the mean
Dispersion value	1.9

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	5.66
Variability estimate	Standard error of the mean
Dispersion value	1.9

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	5.66
Variability estimate	Standard error of the mean
Dispersion value	1.9

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.989
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.37
upper limit	5.29
Variability estimate	Standard error of the mean
Dispersion value	2.72

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	3.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	11.2
Variability estimate	Standard error of the mean
Dispersion value	3.77

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.17
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	13.91
Variability estimate	Standard error of the mean
Dispersion value	4.17

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	3.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	11.2
Variability estimate	Standard error of the mean
Dispersion value	3.77

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.989
Method	Normal approximation for two proportions
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.37
upper limit	5.29
Variability estimate	Standard error of the mean
Dispersion value	2.72

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.091
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	16.52
Variability estimate	Standard error of the mean
Dispersion value	4.53

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.353
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	17.47
Variability estimate	Standard error of the mean
Dispersion value	6.05

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.353
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	17.47
Variability estimate	Standard error of the mean
Dispersion value	6.05

<b>Statistical analysis title</b>	Analysis of ASDAS Inactive Disease at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.228
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.73
upper limit	19.81
Variability estimate	Standard error of the mean
Dispersion value	6.26

### Secondary: Change from Baseline in BASDAI Total Score at Week 2, 4, 8 and 12

End point title	Change from Baseline in BASDAI Total Score at Week 2, 4, 8 and 12
End point description:	
<p>BASDAI is a validated self-assessment tool used to determine disease activity in participant with Ankylosing Spondylitis. Utilizing a Numerical Rating Scale (NRS) of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is calculated by computing the mean of questions 5 and 6 and adding it to the sum of questions (Q)1-4. This score is then divided by 5. <math>BASDAI = (Q1 + Q2 + Q3 + Q4 + [Q5 + Q6/2])/5</math>. The final BASDAI score averages the individual assessments for a final score range of 0-10. Negative values indicate improvement. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 2, Week 4, Week 8, Week 12	

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	-1.45 (± 0.219)	-1.53 (± 0.217)	-1.24 (± 0.219)	-1.42 (± 0.219)
Week 4	-1.9 (± 0.242)	-1.93 (± 0.24)	-1.84 (± 0.242)	-1.6 (± 0.243)
Week 8	-2.16 (± 0.268)	-2.39 (± 0.267)	-2.35 (± 0.271)	-1.87 (± 0.271)
Week 12	-2.75 (± 0.277)	-2.88 (± 0.276)	-2.68 (± 0.281)	-1.85 (± 0.283)

### Statistical analyses



<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.926
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.31

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.718
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.308

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.57
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	0.31

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.384
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.343

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.334
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.341

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.474
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.343

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.445
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.04
upper limit	0.46
Variability estimate	Standard error of the mean
Dispersion value	0.381

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.174
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.38

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.217
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.383

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.024
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.396

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.396

<b>Statistical analysis title</b>	Analysis of BASDAI Total Score at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.038
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.399

### Secondary: Percentage of Participants Achieving a 50% Improvement in BASDAI Response from Baseline (BASDAI 50) at Weeks 2, 4, 8 and 12

End point title	Percentage of Participants Achieving a 50% Improvement in BASDAI Response from Baseline (BASDAI 50) at Weeks 2, 4, 8 and 12
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#### End point description:

BASDAI is a validated self-assessment tool used to determine disease activity in participant with Ankylosing Spondylitis. Utilizing a NRS of 0-10 (0 = none and 10 = very severe) participant's answered 6 questions measuring discomfort, pain and fatigue. The BASDAI score is calculated by computing the mean of questions 5 and 6 and adding it to the sum of questions (Q)1-4. This score is then divided by 5. The final BASDAI score range from 0-10. A positive response was defined as a 50% improvement in the BASDAI from baseline. Analysis population is the FAS, n is the number of responders at each visit.

End point type	Secondary
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#### End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Percentage of participants				
number (not applicable)				
Week 2 (n=6, 11, 7, 8)	11.54	21.15	13.46	15.69
Week 4 (n=15, 12, 15, 11)	28.85	23.08	28.85	21.57
Week 8 (n=18, 17, 21, 14)	34.62	32.69	40.38	27.45
Week 12 (n=24, 22, 22, 12)	46.15	42.31	42.31	23.53

### Statistical analyses

Statistical analysis title	Analysis of BASDAI 50 at Week 2
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#### Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
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Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.539
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	-4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.38
upper limit	9.08
Variability estimate	Standard error of the mean
Dispersion value	6.75

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.473
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.46
upper limit	20.4
Variability estimate	Standard error of the mean
Dispersion value	7.62

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.749
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	-2.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.85
upper limit	11.4
Variability estimate	Standard error of the mean
Dispersion value	6.95

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.393
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.43
upper limit	23.98
Variability estimate	Standard error of the mean
Dispersion value	8.52

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.854
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.57
upper limit	17.59
Variability estimate	Standard error of the mean
Dispersion value	8.2



<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.393
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.43
upper limit	23.98
Variability estimate	Standard error of the mean
Dispersion value	8.52

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.43
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	7.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.65
upper limit	24.97
Variability estimate	Standard error of the mean
Dispersion value	9.09

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.561
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	5.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.44
upper limit	22.92
Variability estimate	Standard error of the mean
Dispersion value	9.02

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.162
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	12.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	31.04
Variability estimate	Standard error of the mean
Dispersion value	9.24

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.013
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	22.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.76
upper limit	40.49
Variability estimate	Standard error of the mean
Dispersion value	9.11

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.038
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	18.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	36.55
Variability estimate	Standard error of the mean
Dispersion value	9.07

<b>Statistical analysis title</b>	Analysis of BASDAI 50 at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.038
Method	Normal approximation for two proportions
Parameter estimate	Risk difference (RD)
Point estimate	18.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	36.55
Variability estimate	Standard error of the mean
Dispersion value	9.07

## Secondary: Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Weeks 2, 4, 8 and 12

End point title	Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) at Weeks 2, 4, 8 and 12
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End point description:

BASFI is a validated self-assessment tool that determines the degree of physical functional limitation in Ankylosing Spondylitis. Utilizing a NRS of 0-10 (0=easy, 10=impossible), participants answered 10 questions assessing their ability in completing normal daily activities or physically demanding activities. The BASFI score is a mean score of the 10 questions with lower scores indicating better physical function. The higher the negative value the better the improvement. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	-1.12 (± 0.192)	-1.16 (± 0.191)	-0.86 (± 0.192)	-0.74 (± 0.192)
Week 4	-1.36 (± 0.21)	-1.61 (± 0.208)	-1.32 (± 0.21)	-1.02 (± 0.21)
Week 8	-1.61 (± 0.247)	-2.07 (± 0.246)	-1.72 (± 0.249)	-1.38 (± 0.249)
Week 12	-1.9 (± 0.261)	-2.39 (± 0.26)	-2.24 (± 0.264)	-1.43 (± 0.266)

## Statistical analyses

Statistical analysis title	Analysis of BASFI at Week 2
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Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.164
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.38

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.272

<b>Statistical analysis title</b>	Analysis of BASFI at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.129
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.271

<b>Statistical analysis title</b>	Analysis of BASFI at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.66
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.272

<b>Statistical analysis title</b>	Analysis of BASFI at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.256
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.297

<b>Statistical analysis title</b>	Analysis of BASFI at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.048
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.296

<b>Statistical analysis title</b>	Analysis of BASFI at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.318
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.297

<b>Statistical analysis title</b>	Analysis of BASFI at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.522
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.47
Variability estimate	Standard error of the mean
Dispersion value	0.35

<b>Statistical analysis title</b>	Analysis of BASFI at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.35

<b>Statistical analysis title</b>	Analysis of BASFI at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.337
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	0.36
Variability estimate	Standard error of the mean
Dispersion value	0.352

<b>Statistical analysis title</b>	Analysis of BASFI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.214
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.373



<b>Statistical analysis title</b>	Analysis of BASFI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.011
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.372

<b>Statistical analysis title</b>	Analysis of BASFI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.031
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.375

## **Secondary: Change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) at Weeks 2, 4, 8 and 12**

End point title	Change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) at Weeks 2, 4, 8 and 12
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**End point description:**

BASMI is an objective measure of spinal mobility and was completed by a blinded assessor. The BASMI score is composed of 5 clinical measures: cervical rotation, intermalleolar distance, modified Schober's test, lateral flexion and tragus to wall distance. The derived score used the average of the 5 assessments on a scale of 0-10 scale with higher scores indicating more impairment of spinal mobility. BASMI was analyzed using the linear function method. The higher the negative value the better the improvement. Analysis population is the FAS, when change from baseline is analysed FAS requires that participants have a baseline and at least one post-baseline measurement.

End point type	Secondary
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**End point timeframe:**

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	-0.09 (± 0.075)	-0.24 (± 0.075)	-0.22 (± 0.075)	-0.09 (± 0.075)
Week 4	-0.15 (± 0.083)	-0.24 (± 0.083)	-0.26 (± 0.084)	-0.14 (± 0.084)
Week 8	-0.34 (± 0.095)	-0.4 (± 0.095)	-0.48 (± 0.096)	-0.19 (± 0.096)
Week 12	-0.33 (± 0.109)	-0.42 (± 0.109)	-0.55 (± 0.111)	-0.16 (± 0.112)

**Statistical analyses**

<b>Statistical analysis title</b>	Analysis of BASMI at Week 2
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**Statistical analysis description:**

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.982
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.106

<b>Statistical analysis title</b>	Analysis of BASMI at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.151
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.106

<b>Statistical analysis title</b>	Analysis of BASMI at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.205
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.106

<b>Statistical analysis title</b>	Analysis of BASMI at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.898
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.118

<b>Statistical analysis title</b>	Analysis of BASMI at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.37
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.118

<b>Statistical analysis title</b>	Analysis of BASMI at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.288
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.119

<b>Statistical analysis title</b>	Analysis of BASMI at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.242
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.135

<b>Statistical analysis title</b>	Analysis of BASMI at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.135

<b>Statistical analysis title</b>	Analysis of BASMI at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.031
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.136

<b>Statistical analysis title</b>	Analysis of BASMI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.28
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.157

<b>Statistical analysis title</b>	Analysis of BASMI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.099
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.157

<b>Statistical analysis title</b>	Analysis of BASMI at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.158

### **Secondary: Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Weeks 4, 8 and 12**

End point title	Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) at Weeks 4, 8 and 12
End point description: Assessment of enthesitis of 13 sites was performed in the following, 1st costochondral joint left and right, 7th costochondral joint left and right, posterior superior iliac spine left and right, anterior superior iliac spine left and right, iliac crest left and right, 5th lumbar spinous process and proximal insertion of Achilles tendon left and right. Each site was graded for the presence (1) and absence (0) of tenderness yielding total MASES ranging from 0 (no tenderness) to 13 (worst possible score; severe tenderness).	
End point type	Secondary
End point timeframe: Baseline, Week 4, Week 8, Week 12	

<b>End point values</b>	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	50	50
Units: Units on a scale				
least squares mean (standard error)				
Week 4	-0.16 (± 0.272)	-0.93 (± 0.271)	-0.89 (± 0.274)	-0.11 (± 0.275)
Week 8	-0.79 (± 0.289)	-1.19 (± 0.289)	-0.97 (± 0.295)	-0.54 (± 0.292)
Week 12	-0.66 (± 0.259)	-1.37 (± 0.259)	-1.24 (± 0.263)	-0.34 (± 0.265)

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of MASES at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.895
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.387

<b>Statistical analysis title</b>	Analysis of MASES at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID



Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.033
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.386

<b>Statistical analysis title</b>	Analysis of MASES at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.044
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.388

<b>Statistical analysis title</b>	Analysis of MASES at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.53
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.411

<b>Statistical analysis title</b>	Analysis of MASES at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.114
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.411

<b>Statistical analysis title</b>	Analysis of MASES at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.297
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.415

<b>Statistical analysis title</b>	Analysis of MASES at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.377
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.37

<b>Statistical analysis title</b>	Analysis of MASES at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.77
upper limit	-0.31
Variability estimate	Standard error of the mean
Dispersion value	0.37

<b>Statistical analysis title</b>	Analysis of MASES at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.373

## Secondary: Extra-Articular Involvement from Specific Ankylosing Spondylitis Medical History

End point title	Extra-Articular Involvement from Specific Ankylosing Spondylitis Medical History
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End point description:

Participants were assessed at Baseline, Week 12 and Week 16 (Follow-up) to determine if they had specific Ankylosing Spondylitis medical history or changes in specific Ankylosing Spondylitis medical history which included: Inflammatory Bowel Disease (IBD), Peripheral Articular Involvement (PAI; as assessed by swollen joint count), psoriasis (PSO) and uveitis (UVE). n=number of participants completing the Specific Medical History Assessment at each visit.

End point type	Secondary
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End point timeframe:

Baseline, Week 12 and Follow-up

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	6	4
Units: Percentage of Participants				
number (not applicable)				
IBD: Never: Baseline (n=6, 9, 6, 4)	100	88.9	100	100
IBD: Past But Not Active: Baseline (n=6, 9, 6, 4)	0	0	0	0
IBD: Currently Active: Baseline (n=6, 9, 6, 4)	0	11.1	0	0
IBD: New Condition: Baseline (n=6, 9, 6, 4)	0	0	0	0
IBD: Never: Week 4 (n=4, 7, 3, 2)	100	100	100	100
IBD: Past But Not Active: Week 4 (n=4, 7, 3, 2)	0	0	0	0
IBD: Currently Active: Week 4 (n=4, 7, 3, 2)	0	0	0	0
IBD: New Condition: Week 4 (n=4, 7, 3, 2)	0	0	0	0
IBD: Never: Week 8 (n=2, 6, 2, 4)	100	100	100	100

IBD: Past But Not Active: Week 8 (n=2, 6, 2, 4)	0	0	0	0
IBD: Currently Active: Week 8 (n=2, 6, 2, 4)	0	0	0	0
IBD: New Condition: Week 8 (n=2, 6, 2, 4)	0	0	0	0
IBD: Never: Week 12 (n=5, 6, 2, 3)	100	100	100	100
IBD: Past But Not Active: Week 12 (n=5, 6, 2, 3)	0	0	0	0
IBD: Currently Active: Week 12 (n=5, 6, 2, 3)	0	0	0	0
IBD: New Condition: Week 12 (n=5, 6, 2, 3)	0	0	0	0
IBD: Never: Follow-up (n=3, 6, 4, 2)	100	100	100	100
IBD: Past But Not Active: Follow-up (n=3,6,4,2)	0	0	0	0
IBD: Currently Active: Follow-up (n=3, 6, 4, 2)	0	0	0	0
IBD: New Condition: Follow-up (n=3, 6, 4, 2)	0	0	0	0
PAI: Never: Baseline (n=6, 9, 6, 4)	33.3	44.4	0	25
PAI: Past But Not Active: Baseline (n=6, 9, 6, 4)	0	0	16.7	0
PAI: Currently Active: Baseline (n=6, 9, 6, 4)	66.7	44.4	66.7	75
PAI: New condition: Baseline (n=6, 9, 6, 4)	0	11.1	16.7	0
PAI: Never: Week 4 (n=4, 7, 3, 2)	0	28.6	0	0
PAI: Past But Not Active: Week 4 (n=4, 7, 3, 2)	0	14.3	33.3	0
PAI: Currently Active: Week 4 (n=4, 7, 3, 2)	100	57.1	66.7	100
PAI: New condition: Week 4 (n=4, 7, 3, 2)	0	0	0	0
PAI: Never: Week 8 (n=2, 6, 2, 4)	0	50	0	0
PAI: Past But Not Active: Week 8 (n=2, 6, 2, 4)	0	0	50	0
PAI: Currently Active: Week 8 (n=2, 6, 2, 4)	100	50	50	100
PAI: New Condition: Week 8 (n=2, 6, 2, 4)	0	0	0	0
PAI: Never: Week 12 (n=5, 5, 2, 3)	20	40	0	0
PAI: Past But Not Active: Week 12 (n=5, 5, 2, 3)	0	0	0	0
PAI: Currently Active: Week 12 (n=5, 5, 2, 3)	40	60	100	100
PAI: New Condition: Week 12 (n=5, 5, 2, 3)	40	0	0	0
PAI: Never: Follow-up (n=3, 6, 4, 2)	0	50	25	0
PAI: Past But Not Active: Follow-up (n=3,6,4,2)	0	0	25	0
PAI: Currently Active: Follow-up (n=3, 6, 4, 2)	66.7	50	50	100
PAI: New Condition: Follow-up (n=3, 6, 4, 2)	33.3	0	0	0
PSO: Never: Baseline (n=6, 9, 6, 4)	100	88.9	83.3	75
PSO: Past But Not Active: Baseline (n=6, 9, 6, 4)	0	0	0	0
PSO: Currently Active: Baseline (n=6, 9, 6, 4)	0	11.1	16.7	25

PSO: New Condition: Baseline (n=6, 9, 6, 4)	0	0	0	0
PSO: Never: Week 4 (n=4, 7, 3, 2)	100	85.7	66.7	100
PSO: Past But Not Active: Week 4 (n=4, 7, 3, 2)	0	0	0	0
PSO: Currently Active: Week 4 (n=4, 7, 3, 2)	0	14.3	33.3	0
PSO: New Condition: Week 4 (n=4, 7, 3, 2)	0	0	0	0
PSO: Never: Week 8 (n=2, 6, 2, 4)	100	83.3	50	100
PSO: Past But Not Active: Week 8 (n=2, 6, 2, 4)	0	0	0	0
PSO: Currently Active: Week 8 (n=2, 6, 2, 4)	0	16.7	50	0
PSO: New Condition: Week 8 (n=2, 6, 2, 4)	0	0	0	0
PSO: Never: Week 12 (n=5, 6, 2, 3)	80	83.3	100	100
PSO: Past But Not Active: Week 12 (n=5, 6, 2, 3)	20	0	0	0
PSO: Currently Active: Week 12 (n=5, 6, 2, 3)	0	16.7	0	0
PSO: New Condition: Week 12 (n=5, 6, 2, 3)	0	0	0	0
PSO: Never: Follow-up (n=3, 6, 4, 2)	100	83.3	100	100
PSO: Past But Not Active: Follow-up (n=3,6,4,2)	0	0	0	0
PSO: Currently Active: Follow-up (n=3, 6, 4, 2)	0	16.7	0	0
PSO: New Condition: Follow-up (n=3, 6, 4, 2)	0	0	0	0
UVE: Never: Baseline (n=6, 9, 6, 4)	50	55.6	83.3	100
UVE: Past But Not Active: Baseline (n=6, 9, 6, 4)	16.7	33.3	0	0
UVE: Currently Active: Baseline (n=6, 9, 6, 4)	33.3	11.1	16.7	0
UVE: New Condition: Baseline (n=6, 9, 6, 4)	0	0	0	0
UVE: Never: Week 4 (n=4, 7, 3, 2)	75	71.4	66.7	100
UVE: Past But Not Active: Week 4 (n=4,7,3,2)	25	28.6	33.3	0
UVE: Currently Active: Week 4 (n=4, 7, 3, 2)	0	0	0	0
UVE: New Condition: Week 4 (n=4, 7, 3, 2)	0	0	0	0
UVE: Never: Week 8 (n=2, 6, 2, 4)	100	50	50	100
UVE: Past But Not Active: Week 8 (n=2, 6, 2, 4)	0	50	50	0
UVE: Currently Active: Week 8 (n=2, 6, 2, 4)	0	0	0	0
UVE: New Condition: Week 8 (n=2, 6, 2, 4)	0	0	0	0
UVE: Never: Week 12 (n=5, 6, 2, 3)	40	66.7	50	100
UVE: Past But Not Active: Week 12 (n=5, 6, 2, 3)	60	33.3	50	0
UVE: Currently Active: Week 12 (n=5, 6, 2, 3)	0	0	0	0
UVE: New Condition: Week 12 (n=5, 6, 2, 3)	0	0	0	0
UVE: Never: Follow-up (n=3, 6, 4, 2)	100	50	50	100

UVE: Past But Not Active: Follow-up (n=3,6,4,2)	0	33.3	25	0
UVE: Currently Active: Follow-up (n=3, 6, 4, 2)	0	16.7	0	0
UVE: New Condition: Follow-up (n=3, 6, 4, 2)	0	0	25	0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline of Total Swollen Joint Count at Weeks 2, 4, 8, and 12

End point title	Change from Baseline of Total Swollen Joint Count at Weeks 2, 4, 8, and 12
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End point description:

This assessment was performed by the blinded assessor using the following scale: Present/Absent/Not Done/Not Applicable (to be used for artificial or missing joints) for determination of the total number of swollen joints. Forty-four joints were assessed for swelling on left and right side and included the following: sternoclaviculars, acromioclaviculars, shoulders, elbows, wrists, metacarpophalangeals (I, II, III, IV, V), thumb interphalangeal, proximal interphalangeals (II, III, IV, V), knees, ankles, and metatarsophalangeals (I, II, III, IV, V). Artificial joints were not assessed. A negative change means improvement.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	-0.53 (± 0.293)	0.23 (± 0.291)	-1.2 (± 0.292)	-0.43 (± 0.293)
Week 4	-0.87 (± 0.26)	-0.57 (± 0.259)	-1.23 (± 0.26)	-0.86 (± 0.261)
Week 8	-1.02 (± 0.442)	-0.98 (± 0.442)	-1.28 (± 0.451)	-0.6 (± 0.448)
Week 12	-0.87 (± 0.362)	-0.79 (± 0.362)	-1.4 (± 0.368)	-0.99 (± 0.373)

## Statistical analyses

Statistical analysis title	Analysis of Total Swollen Joint Count at Week 2
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Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
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Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.414

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.113
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	1.47
Variability estimate	Standard error of the mean
Dispersion value	0.413

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 2
Statistical analysis description:	
Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.064
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.77



Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.414

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.972
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.368

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.44
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	1.01
Variability estimate	Standard error of the mean
Dispersion value	0.368

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.311
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.369

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.501
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	0.82
Variability estimate	Standard error of the mean
Dispersion value	0.629

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.543
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.629

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.287
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	0.636

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.82
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	1.14
Variability estimate	Standard error of the mean
Dispersion value	0.519

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.711
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	1.22
Variability estimate	Standard error of the mean
Dispersion value	0.52

<b>Statistical analysis title</b>	Analysis of Total Swollen Joint Count at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.424
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.524

## Secondary: Change from Baseline of Mean Spinal Mobility (Chest Expansion) at Week 2, 4, 8 and 12

End point title	Change from Baseline of Mean Spinal Mobility (Chest Expansion) at Week 2, 4, 8 and 12
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### End point description:

Chest expansion, measured in centimetres (cm), is defined as the difference in the thoracic circumference during full expiration versus full inspiration. This was measured at the 4th intercostal space. The difference between maximal inspiration and expiration of the two attempts was recorded. The better of the two attempts was used to calculate chest expansion. Missing data at Week 12 were imputed by LOCF if data at an early visit (discontinuation visit) were available.

End point type	Secondary
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### End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	0.3 (± 0.144)	0.35 (± 0.143)	-0.03 (± 0.144)	0.24 (± 0.144)
Week 4	0.54 (± 0.164)	0.13 (± 0.162)	0.13 (± 0.164)	0.38 (± 0.165)
Week 8	0.52 (± 0.178)	0.35 (± 0.178)	0.15 (± 0.182)	0.13 (± 0.181)
Week 12	0.69 (± 0.187)	0.49 (± 0.187)	0.13 (± 0.19)	0.31 (± 0.193)

## Statistical analyses

Statistical analysis title	Analysis of Mean Spinal Mobility at Week 2
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### Statistical analysis description:

Week 2

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.785
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.46

Variability estimate	Standard error of the mean
Dispersion value	0.203

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.605
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.51
Variability estimate	Standard error of the mean
Dispersion value	0.203

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.175
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.204

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 4
Statistical analysis description: Week 4	

Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.482
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.62
Variability estimate	Standard error of the mean
Dispersion value	0.232

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.288
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.231

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.278
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.233

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.134
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.88
Variability estimate	Standard error of the mean
Dispersion value	0.254

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.397
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.254



<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 8
Statistical analysis description: Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.964
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.52
Variability estimate	Standard error of the mean
Dispersion value	0.257

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.155
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.91
Variability estimate	Standard error of the mean
Dispersion value	0.269

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.491
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.269

<b>Statistical analysis title</b>	Analysis of Mean Spinal Mobility at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.515
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.36
Variability estimate	Standard error of the mean
Dispersion value	0.271

### **Secondary: Change from Baseline to Week 12 in Short-Form-36 Health Survey (SF-36) Physical and Mental Health Scores at Week 12**

End point title	Change from Baseline to Week 12 in Short-Form-36 Health Survey (SF-36) Physical and Mental Health Scores at Week 12
End point description:	
SF-36 is a standardized survey evaluating 8 aspects of functional health and wellbeing: physical and social functioning, physical and emotional role limitations, bodily pain, general health, vitality, mental health. The score for a section is an average of the individual question scores, which are scaled 0-100 (0=no functioning, 100=highest level of functioning). Missing data at Week 12 were imputed by LOCF if data at an early visit (discontinuation visit) were available.	
End point type	Secondary
End point timeframe:	
Baseline, Week 12	

<b>End point values</b>	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Units on a scale				
least squares mean (standard error)				
Week 12 Physical Health Score	6.34 (± 0.923)	6.49 (± 0.914)	7.05 (± 0.943)	2.69 (± 0.932)
Week 12 Mental Health Score	2.08 (± 1.306)	4.15 (± 1.294)	3.71 (± 1.336)	2.41 (± 1.318)

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of SF-36 Physical Health Score at Week 12
Statistical analysis description: Physical Health Score	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	6.24
Variability estimate	Standard error of the mean
Dispersion value	1.312

<b>Statistical analysis title</b>	Analysis of SF-36 Physical Health Score at Week 12
Statistical analysis description: Physical Health Score	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	6.37
Variability estimate	Standard error of the mean
Dispersion value	1.305

<b>Statistical analysis title</b>	Analysis of SF-36 Physical Health Score at Week 12
Statistical analysis description: Physical Health Score	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.74
upper limit	6.98
Variability estimate	Standard error of the mean
Dispersion value	1.328

<b>Statistical analysis title</b>	Analysis of SF-36 Mental Health Score at Week 12
Statistical analysis description: Mental Health Score	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.857
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3.33
Variability estimate	Standard error of the mean
Dispersion value	1.857

<b>Statistical analysis title</b>	Analysis of SF-36 Mental Health Score at Week 12
Statistical analysis description: Mental Health Score	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.35
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	5.37
Variability estimate	Standard error of the mean
Dispersion value	1.848

<b>Statistical analysis title</b>	Analysis of SF-36 Mental Health Score at Week 12
Statistical analysis description: Mental Health Score	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.49
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	5
Variability estimate	Standard error of the mean
Dispersion value	1.876

## **Secondary: Change from Baseline in EuroQol EQ-5D Health State Profile (EQ-5D) Utility Score at Week 12**

End point title	Change from Baseline in EuroQol EQ-5D Health State Profile (EQ-5D) Utility Score at Week 12
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EQ-5D: participant rated questionnaire to assess health-related quality of life in terms of single utility score. Health state profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression; Scale range 1 to 3 (1=better health state [no problems], 3=worst health state [confined to bed]).

End point timeframe:

Baseline, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	52	52	51
Units: Units on a scale				
least squares mean (standard error)	0.17 (± 0.034)	0.16 (± 0.034)	0.22 (± 0.035)	0.1 (± 0.034)

## Statistical analyses

Statistical analysis title	Analysis of EQ-5D Utility Score at Week 12
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.125
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.048

<b>Statistical analysis title</b>	Analysis of EQ-5D Utility Score at Week 12
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.207
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.048

<b>Statistical analysis title</b>	Analysis of EQ-5D Utility Score at Week 12
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.013
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.049

### **Secondary: Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Weeks 2, 4, 8 and 12**

End point title	Change from Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Weeks 2, 4, 8 and 12
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#### End point description:

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

End point type	Secondary
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#### End point timeframe:

Baseline, Week 2, Week 4, Week 8, Week 12

End point values	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	51
Units: Units on a scale				
least squares mean (standard error)				
Week 2	3.62 ( $\pm$ 0.871)	1.97 ( $\pm$ 0.871)	2.17 ( $\pm$ 0.875)	1.9 ( $\pm$ 0.872)
Week 4	4.25 ( $\pm$ 0.931)	3.67 ( $\pm$ 0.927)	2.8 ( $\pm$ 0.937)	2.71 ( $\pm$ 0.938)
Week 8	4.54 ( $\pm$ 1.039)	4.81 ( $\pm$ 1.039)	4.19 ( $\pm$ 1.061)	2.85 ( $\pm$ 1.053)
Week 12	4.74 ( $\pm$ 1.145)	7.03 ( $\pm$ 1.145)	7.58 ( $\pm$ 1.166)	3.08 ( $\pm$ 1.178)

## Statistical analyses

Statistical analysis title	Analysis of FACIT-F Score at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.163
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	4.15
Variability estimate	Standard error of the mean
Dispersion value	1.232

Statistical analysis title	Analysis of FACIT-F Score at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.955
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07



Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	2.5
Variability estimate	Standard error of the mean
Dispersion value	1.232

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 2
Statistical analysis description: Week 2	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.826
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	2.71
Variability estimate	Standard error of the mean
Dispersion value	1.237

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 4
Statistical analysis description: Week 4	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.246
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	4.14
Variability estimate	Standard error of the mean
Dispersion value	1.322

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.467
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	3.56
Variability estimate	Standard error of the mean
Dispersion value	1.318

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 4
Statistical analysis description:	
Week 4	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.948
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	1.328

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.255
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	4.61
Variability estimate	Standard error of the mean
Dispersion value	1.479

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.187
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	4.87
Variability estimate	Standard error of the mean
Dispersion value	1.479

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 8
Statistical analysis description:	
Week 8	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.373
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	4.29
Variability estimate	Standard error of the mean
Dispersion value	1.497

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 2 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.313
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	4.9
Variability estimate	Standard error of the mean
Dispersion value	1.643

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 12
Statistical analysis description: Week 12	
Comparison groups	Tofacitinib 5 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	7.19
Variability estimate	Standard error of the mean
Dispersion value	1.642

<b>Statistical analysis title</b>	Analysis of FACIT-F Score at Week 12
Statistical analysis description:	
Week 12	
Comparison groups	Tofacitinib 10 mg BID v Placebo BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.007
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	7.78
Variability estimate	Standard error of the mean
Dispersion value	1.66

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From informed consent through and including 28 calendar days after the last administration of the investigational product.

Adverse event reporting additional description:

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

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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### Reporting groups

Reporting group title	Tofacitinib 2 mg BID
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Reporting group description:

Participants were administered 4 tablets (two 1 mg tablets of tofacitinib along with two 5 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.

Reporting group title	Tofacitinib 5 mg BID
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Reporting group description:

Participants were administered 4 tablets (one 5 mg tablet of tofacitinib, one 5 mg and two 1 mg matching placebo tablets) orally BID (in the AM and PM) for a total of 12 weeks.

Reporting group title	Tofacitinib 10 mg BID
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Reporting group description:

Participants were administered 4 tablets (two 5 mg tablets of tofacitinib and two 1 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.

Reporting group title	Placebo BID
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Reporting group description:

Participants were administered 4 tablets (two 1 mg placebo tablets and two 5 mg matching placebo tablets) orally twice a day (in the AM and PM) for a total of 12 weeks.

Serious adverse events	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Tendon injury			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			

Foetal death			
subjects affected / exposed <sup>[1]</sup>	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	0 / 52 (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
Reproductive system and breast disorders			
Uterine spasm			
subjects affected / exposed <sup>[2]</sup>	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed <sup>[3]</sup>	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Placebo BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Tendon injury			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			

Foetal death			
subjects affected / exposed <sup>[1]</sup>	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine spasm			
subjects affected / exposed <sup>[2]</sup>	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			
subjects affected / exposed <sup>[3]</sup>	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

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



<b>Non-serious adverse events</b>	Tofacitinib 2 mg BID	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 52 (28.85%)	10 / 52 (19.23%)	13 / 52 (25.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 52 (1.92%)	2 / 52 (3.85%)	0 / 52 (0.00%)
occurrences (all)	1	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 52 (0.00%)	2 / 52 (3.85%)	1 / 52 (1.92%)
occurrences (all)	0	2	1
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	2 / 52 (3.85%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 52 (3.85%)	2 / 52 (3.85%)	2 / 52 (3.85%)
occurrences (all)	2	2	2
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed <sup>[4]</sup>	0 / 18 (0.00%)	0 / 13 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 52 (5.77%)	0 / 52 (0.00%)	2 / 52 (3.85%)
occurrences (all)	3	0	2
Diarrhoea			
subjects affected / exposed	2 / 52 (3.85%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences (all)	3	1	0
Mouth ulceration			
subjects affected / exposed	2 / 52 (3.85%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			

Balanoposthitis subjects affected / exposed <sup>[5]</sup> occurrences (all)	1 / 34 (2.94%) 1	0 / 39 (0.00%) 0	0 / 38 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 52 (0.00%) 0	0 / 52 (0.00%) 0
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	1 / 52 (1.92%) 1	2 / 52 (3.85%) 2
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	2 / 52 (3.85%) 3	0 / 52 (0.00%) 0
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	0 / 52 (0.00%) 0	1 / 52 (1.92%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4	4 / 52 (7.69%) 4	2 / 52 (3.85%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 5	0 / 52 (0.00%) 0	3 / 52 (5.77%) 3
Vaginitis bacterial subjects affected / exposed <sup>[6]</sup> occurrences (all)	0 / 18 (0.00%) 0	0 / 13 (0.00%) 0	0 / 14 (0.00%) 0
Vulvovaginal mycotic infection subjects affected / exposed <sup>[7]</sup> occurrences (all)	1 / 18 (5.56%) 1	0 / 13 (0.00%) 0	0 / 14 (0.00%) 0

<b>Non-serious adverse events</b>	Placebo BID		
Total subjects affected by non-serious adverse events subjects affected / exposed	14 / 51 (27.45%)		
Investigations			

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Injury, poisoning and procedural complications Ligament sprain subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)  Headache subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2  1 / 51 (1.96%) 1		
Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed <sup>[4]</sup> occurrences (all)	1 / 19 (5.26%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Mouth ulceration subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1  1 / 51 (1.96%) 1  1 / 51 (1.96%) 1		
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed <sup>[5]</sup> occurrences (all)	0 / 32 (0.00%) 0		
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)  Nasopharyngitis subjects affected / exposed occurrences (all)  Upper respiratory tract infection subjects affected / exposed occurrences (all)  Vaginitis bacterial subjects affected / exposed <sup>[6]</sup> occurrences (all)  Vulvovaginal mycotic infection subjects affected / exposed <sup>[7]</sup> occurrences (all)	2 / 51 (3.92%) 2  3 / 51 (5.88%) 3  1 / 51 (1.96%) 1  1 / 19 (5.26%) 1  0 / 19 (0.00%) 0		

Notes:

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the exception of balanoposthitis which only male participants were counted as exposed to.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: only female participants were counted as exposed to these adverse events, with the

exception of balanoposthitis which only male participants were counted as exposed to.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2013	Description: Clarification of and updates to some inclusion and exclusion criteria. Addition of opportunistic infections to the discontinuation criteria and clarification of when an investigator could discontinue a participant in the event of serious or severe AEs. New sponsor standard wording providing clarity on the method of access to the sponsor Qualified Medical Personnel and medical coverage. Clarification of total blood draw volume anticipated during the study. Section on retained pharmacogenomics samples (banked biospecimens) and markers of drug response was updated. Clarification of SAE reporting requirements for protocol specified SAEs. Additional AE sections related to infections. Updates to communication of results by Pfizer.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported