Clinical trial results:
A Phase 3b/4, Multi-Center, Double-Blind, Randomized, Parallel Group Study of Tofacitinib (CP-690,550) in Subjects With Ulcerative Colitis in Stable Remission

Summary

EudraCT number	2017-002274-39
Trial protocol	SK CZ BE HU NL GB AT ES IT
Global end of trial date	18 March 2022

Results information

Result version number	v1 (current)
This version publication date	10 March 2023
First version publication date	10 March 2023

Trial information

Trial identification

Sponsor protocol code	A3921288

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03281304
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 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of tofacitinib in subjects in stable remission on 10 milligram (mg) twice daily (BID) who decrease the dose to and remain on 5 mg BID ("5 mg BID dose group") compared to subjects remaining on 10 mg BID.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Slovakia: 13
Country: Number of subjects enrolled	South Africa: 9
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Ukraine: 12
Country: Number of subjects enrolled	United Kingdom: 1

Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	140
EEA total number of subjects	48

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	122
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study enrolled subjects from A3921139(NCT01470612) who were on tofacitinib 10 mg BID for at least 2 consecutive years, who were in stable remission for at least 6 months prior to baseline of A3921288, not receiving any corticosteroid treatment to treat their ulcerative colitis (UC) for at least 4 weeks prior to enrollment.

Pre-assignment

Screening details:

The Baseline visit of this study was the last visit in study A3921139. All procedures done at the last visit in A3921139 for subjects enrolled into this study were used as the Baseline data for this study. The study was conducted in 18 countries from 16-Nov-2017 to 18-Mar-2022.

Period 1

Period 1 title	Treatment Phase (up to 42 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

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

Arm description:

Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.

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

Dosage and administration details:

Subjects received tofacitinib 5 mg tablet orally BID.

Arm title	Tofacitinib 10 mg BID

Arm description:

Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.

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

Dosage and administration details:

Subjects received tofacitinib 10 mg tablet orally BID.

Number of subjects in period 1	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Started	70	70
Completed	36	27
Not completed	34	43
Adverse event, not serious	3	1
Consent withdrawn by subject	5	12
Death	-	1
Pregnancy	1	-
Study terminated by sponsor	15	16
Adverse event, serious non-fatal	7	8
Unspecified	-	2
Adverse event, serious (fatality unknown)	-	1
Lack of efficacy	3	2

Period 2

Period 2 title	Follow-up Phase (up to 4 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Tofacitinib 5 mg BID

Arm description:

Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.

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

Dosage and administration details:

Subjects received tofacitinib 5 mg tablet orally BID.

Arm title	Tofacitinib 10 mg BID

Arm description:

Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.

Arm type	Experimental

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

Dosage and administration details:

Subjects received tofacitinib 10 mg tablet orally BID.

Number of subjects in period 2	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Started	63	57
Completed	61	56
Not completed	2	1
Unspecified	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	

Reporting group values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Total
Number of subjects	70	70	140
Age Categorical Units: subjects			
<=18 years	0	0	0
Between 18 and 65 years	59	63	122
>=65 years	11	7	18
Age continuous Units: years			
arithmetic mean	47.81	47.81	
standard deviation	± 14.15	± 13.55	-
Sex: Female, Male Units: subjects			
Female	26	22	48
Male	44	48	92
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	15	14	29
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	0	3
White	50	50	100
More than one race	0	1	1
Unknown or Not Reported	2	5	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	68	67	135
Unknown or Not Reported	1	2	3

End points

End points reporting groups

Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, BID up to 42 months. Subjects were followed up to 4 weeks after the last dose.	

Primary: Number of Subjects With Remission Based on Modified Mayo Score at Month 6

End point title	Number of Subjects With Remission Based on Modified Mayo Score at Month 6
End point description:	
Remission as per modified mayo score was defined as an endoscopic subscore of 0 or 1, stool frequency subscore of 0 or 1, and rectal bleeding subscore of 0 at Month 6. Modified mayo score consisted of 3 components: stool frequency subscore, rectal bleeding subscore and endoscopic subscore: higher scores for each score = more severe disease. These scores were summed up to give a total modified mayo score range of 0 to 9; where higher scores indicating more severe disease. Full analysis set (FAS) included all subjects who were randomised and received at least 1 dose of investigational product (IP).	
End point type	Primary
End point timeframe:	
Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects	54	63		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	25

Secondary: Time to Loss of Remission Based on Modified Mayo Score Using Kaplan-Meier Method

End point title	Time to Loss of Remission Based on Modified Mayo Score Using Kaplan-Meier Method

End point description:

Time to loss of remission(flare):time from first drug administration until time of meeting loss of remission criteria based on modified mayo score(MMS). Loss of remission: meeting >=1 criteria: increase from Baseline in rectal bleeding subscore by >=1 point, increase in endoscopic subscore by >=1 point; increase from Baseline in rectal bleeding subscore by >=2 points, endoscopic subscore >0; increase in stool frequency subscore by >=2 points, increase in endoscopic subscore by >=1point; increase in endoscopic subscore by >=2points. MMS included 3 components: stool frequency, rectal bleeding and endoscopic subscores, each subscore graded from 0 to 3 with higher scores for each score=more severe disease. All scores summed up to give total modified mayo score range from 0 to 9; higher scores=more severe disease. FAS: all subjects who were randomised and received at least 1 dose of IP. 999=Median was not estimated due to insufficient number of subjects with event.

End point type	Secondary

End point timeframe:

Up to Month 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Days				
median (full range (min-max))	999 (29 to 1268)	1270 (28 to 1270)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Remission Based on Modified Partial Mayo Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Number of Subjects With Remission Based on Modified Partial Mayo Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Remission as per modified partial mayo score was defined as stool frequency subscore of 0 or 1, and rectal bleeding sub score of 0 at the specified time points. Modified partial mayo scores consisted of 2 components: stool frequency and rectal bleeding: each subscore graded from 0 to 3 with higher scores for each score = more severe disease. These scores were summed up to give a total modified partial mayo score range of 0 to 6; where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 1	62	64		
Month 3	57	65		
Month 6	57	67		
Month 9	52	66		
Month 12	50	61		
Month 15	48	58		
Month 18	45	55		
Month 21	46	51		
Month 24	47	51		
Month 27	43	49		
Month 30	44	46		
Month 33	42	43		
Month 36	42	44		
Month 39	40	37		
Month 42	26	29		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 1: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	13.4

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 3: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	22.8

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	25.2

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 9: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	20

Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	31.8

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 12: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	28.7

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	28.5

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 15: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	27.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 21: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	21.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 24: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	20.4

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 27: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	23.6

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	18.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 33: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	17.2

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 36: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	18.5

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 39: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.2
upper limit	11.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	4.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	19.9

Secondary: Number of Subjects With Remission Based on Total Mayo Score at Months 6, 18, 30 and 42

End point title	Number of Subjects With Remission Based on Total Mayo Score at Months 6, 18, 30 and 42

End point description:

Remission as per total mayo score was defined by a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point and a rectal bleeding subscore of 0. Mayo score is an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and physician global assessment (PGA), each subscore graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a total mayo score range of 0 to 12, where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Months 6, 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 6	53	61		
Month 18	33	47		
Month 30	35	44		
Month 42	22	24		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	24.1

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.6
upper limit	35

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	28.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	18

Secondary: Number of Subjects With Remission Based on Partial Mayo Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Number of Subjects With Remission Based on Partial Mayo Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Remission as per partial mayo score was defined as partial mayo score of 2 points or lower, with no individual subscore exceeding 1 point and a rectal bleeding subscore of 0. Partial mayo score was an instrument designed to measure disease activity of UC without endoscopy. It consisted of 3 subscores: stool frequency, rectal bleeding and PGA with each subscore graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a total partial mayo score ranges from 0 (normal or inactive disease) to 9 (severe disease) with higher scores indicating more severe disease. Full analysis set included all subjects who were randomised and received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 1	62	64		
Month 3	57	65		
Month 6	56	66		
Month 9	52	66		
Month 12	50	61		
Month 15	48	58		
Month 18	44	55		
Month 21	46	50		
Month 24	46	51		
Month 27	42	49		
Month 30	43	46		

Month 33	42	43		
Month 36	42	44		
Month 39	39	37		
Month 42	26	28		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 3: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	22.8

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 1: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	13.4

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	25.6

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 9: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	31.8

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 12: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	28.7

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	29.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 15: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	27.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 21: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	20.6

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 24: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	21.9

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 27: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	25.1

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	4.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	19.7

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 33: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	17.2

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 36: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	18.5

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 39: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.8
upper limit	13.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	18.5

Secondary: Number of Subjects With Remission Based on Modified Mayo Score at Months 18, 30 and 42

End point title	Number of Subjects With Remission Based on Modified Mayo Score at Months 18, 30 and 42

End point description:

Remission as per modified mayo score was defined as an endoscopic subscore of 0 or 1, stool frequency subscore of 0 or 1, and rectal bleeding subscore of 0. Modified mayo score consisted of 3 components: stool frequency subscore, rectal bleeding subscore and endoscopic subscore: higher scores for each score = more severe disease. These scores were summed up to give a total modified mayo score range of 0 to 9; where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Months 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 18	37	48		
Month 30	35	44		
Month 42	23	24		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	30.8

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	16.7

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:	
Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	28.3

Secondary: Change From Baseline in Modified Mayo Score at Month 6

End point title	Change From Baseline in Modified Mayo Score at Month 6
End point description:	
Modified mayo score is an instrument designed to measure disease activity of UC. Modified mayo scores consisted of 3 subscores: stool frequency, rectal bleeding and endoscopic subscore, each subscore graded from 0 to 3 with higher scores indicating more severe disease. These individual scores were summed up to give a total modified mayo score range of 0 to 9, where higher scores indicated more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline, Month 6	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	68		
Units: Units on a scale				
least squares mean (standard error)	0.6 (± 0.2)	0.3 (± 0.2)		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.1

Secondary: Change From Baseline in Modified Mayo Score at Months 18, 30 and 42

End point title	Change From Baseline in Modified Mayo Score at Months 18, 30 and 42

End point description:

Modified mayo score is an instrument designed to measure disease activity of UC. Modified mayo scores consisted of 3 subscores: stool frequency, rectal bleeding and endoscopic subscore, each subscore graded from 0 to 3 with higher scores indicating more severe disease. These individual scores were summed up to give a total modified mayo score range of 0 to 9, where higher scores indicated more severe disease. FAS included all subjects who were randomised and received at least 1 dose of investigational product. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	57		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 18 (n= 48, 57)	0.5 (± 1.3)	0.3 (± 1.5)		
Change at Month 30 (n= 44, 45)	0.3 (± 1.2)	0.1 (± 0.9)		
Change at Month 42 (n= 40, 34)	0.3 (± 0.9)	0.2 (± 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Modified Partial Mayo Score at Months 1, 3 and 6

End point title	Change From Baseline in Modified Partial Mayo Score at Months 1, 3 and 6

End point description:

Modified partial mayo scores consisted of 2 subscores: stool frequency and rectal bleeding with each subscore graded from 0 to 3 with higher scores indicating more severe disease. Individual subscores were summed up to give a total modified partial mayo score range from 0 (normal or inactive disease) to 6 (severe disease) with higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' = subjects evaluable for this endpoint and n = number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe: Baseline, Months 1, 3 and 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	69		
Units: Units on a scale				
least squares mean (standard error)				
Change at Month 1 (n= 67, 66)	0.1 (± 0.1)	0.2 (± 0.1)		
Change at Month 3 (n= 64, 68)	0.2 (± 0.1)	0.1 (± 0.1)		
Change at Month 6 (n= 60, 69)	0.1 (± 0.1)	0.2 (± 0.1)		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2

	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis title	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.3

Secondary: Change From Baseline in Modified Partial Mayo Score at Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Change From Baseline in Modified Partial Mayo Score at Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Modified partial mayo scores consisted of 2 subscores: stool frequency and rectal bleeding with each subscore graded from 0 to 3 with higher scores indicating more severe disease. Individual subscores were summed up to give a total modified partial mayo score range from 0 (normal or inactive disease) to 6 (severe disease) with higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	67		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 9 (n= 53, 67)	0.1 (± 0.7)	0.1 (± 0.6)		
Change at Month 12 (n= 51, 63)	0.1 (± 0.5)	0.1 (± 0.7)		
Change at Month 15 (n= 51, 57)	0.2 (± 0.8)	0.1 (± 0.6)		
Change at Month 18 (n= 47, 56)	0.1 (± 0.6)	0.1 (± 0.8)		
Change at Month 21 (n= 48, 54)	0.1 (± 0.5)	0.2 (± 1.1)		
Change at Month 24 (n= 47, 50)	0.0 (± 0.5)	0.0 (± 0.6)		
Change at Month 27 (n= 45, 48)	0.1 (± 0.5)	0.1 (± 0.7)		
Change at Month 30 (n= 45, 45)	0.1 (± 0.7)	0.0 (± 0.6)		
Change at Month 33 (n= 42, 41)	0.0 (± 0.4)	0.2 (± 0.7)		
Change at Month 36 (n= 43, 41)	0.0 (± 0.5)	0.0 (± 0.5)		
Change at Month 39 (n= 40, 34)	0.0 (± 0.5)	0.0 (± 0.5)		
Change at Month 42 (n= 26, 26)	0.1 (± 0.4)	0.1 (± 0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Mayo Score at Month 6

End point title	Change From Baseline in Total Mayo Score at Month 6

End point description:

Mayo score is an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each sub score graded from 0 to 3 with higher scores indicating more severe disease. Individual subscores were summed up to give a total mayo score range of 0 to 12, where higher scores indicating more severe disease. Full analysis set included all subjects who were randomised and received at least 1 dose of investigational product. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	68		
Units: Units on a scale				
least squares mean (standard error)	0.9 (± 0.2)	0.4 (± 0.3)		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1

Secondary: Change From Baseline in Total Mayo Score at Months 18, 30 and 42

End point title	Change From Baseline in Total Mayo Score at Months 18, 30 and 42

End point description:

Mayo score is an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each sub score graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a total mayo score range of 0 to 12, where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n = number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	57		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 18 (n= 48, 57)	0.7 (± 1.7)	0.4 (± 1.9)		
Change at Month 30 (n= 44, 45)	0.4 (± 1.4)	0.1 (± 1.2)		
Change at Month 42 (n= 40, 34)	0.4 (± 1.2)	0.2 (± 1.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Partial Mayo Score at Months 1, 3 and 6

End point title	Change From Baseline in Partial Mayo Score at Months 1, 3 and 6

End point description:

Partial mayo score was an instrument designed to measure disease activity of UC without endoscopy. It consisted of 3 subscores: stool frequency, rectal bleeding and PGA with each subscore graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a total partial mayo score ranges from 0 (normal or inactive disease) to 9 (severe disease) with higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 1, 3 and 6

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Units on a scale				
least squares mean (standard error)				
Change at Month 1 (n= 67, 66)	0.2 (± 0.1)	0.2 (± 0.1)		
Change at Month 3 (n= 64, 68)	0.3 (± 0.1)	0.2 (± 0.1)		
Change at Month 6 (n= 60,69)	0.3 (± 0.1)	0.3 (± 0.1)		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 1	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description: Month 6	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:	
Month 3	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2

Secondary: Change From Baseline in Partial Mayo Score at Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Change From Baseline in Partial Mayo Score at Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Partial mayo score was an instrument designed to measure disease activity of UC without endoscopy. It consisted of 3 subscores: stool frequency, rectal bleeding and PGA with each subscore graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a total partial mayo score ranges from 0 (normal or inactive disease) to 9 (severe disease) with higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed'=subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	67		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Month 9 (n= 53, 67)	0.2 (± 0.8)	0.2 (± 0.9)		
Change at Month 12 (n= 51, 63)	0.1 (± 0.7)	0.2 (± 0.9)		
Change at Month 15 (n= 51, 57)	0.3 (± 1.2)	0.1 (± 0.8)		
Change at Month 18 (n= 47, 56)	0.2 (± 0.8)	0.2 (± 1.2)		
Change at Month 21 (n= 48, 54)	0.1 (± 0.7)	0.4 (± 1.7)		
Change at Month 24 (n= 46, 50)	0.1 (± 0.6)	0.0 (± 0.8)		
Change at Month 27 (n= 44, 48)	0.1 (± 0.6)	0.1 (± 0.9)		
Change at Month 30 (n= 45, 45)	0.2 (± 0.8)	0.1 (± 0.8)		
Change at Month 33 (n= 42, 41)	0.0 (± 0.5)	0.2 (± 1.0)		
Change at Month 36 (n= 43, 41)	0.0 (± 0.6)	-0.1 (± 0.6)		
Change at Month 39 (n= 39, 34)	0.1 (± 0.6)	-0.1 (± 0.6)		

Change at Month 42 (n= 26,25)	0.1 (± 0.5)	0.2 (± 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Mucosal Healing at Months 6, 18, 30 and 42

End point title	Number of Subjects With Mucosal Healing at Months 6, 18, 30 and 42

End point description:

Mucosal healing in subjects was defined as the mayo endoscopic subscore of 0 or 1. The Mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher scores indicated more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Months 6, 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 6	56	64		
Month 18	43	56		
Month 30	38	47		
Month 42	36	36		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	23.1

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	32.6

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	28.1

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.1
upper limit	16.1

Secondary: Number of Subjects With Clinical Response Based on Mayo Score at Months 6, 18, 30 and 42

End point title	Number of Subjects With Clinical Response Based on Mayo Score at Months 6, 18, 30 and 42

End point description:

Clinical response was defined as a decrease from baseline in mayo score of at least 3 points and at least 30 percent, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1. Mayo score is an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each sub score graded from 0 to 3 with higher scores indicating more severe disease. PGA included 3 criteria: subject's recollection of abdominal discomfort, general sense of wellbeing and other observations such as physical findings and performance status. Individual subscores were summed up to give a mayo score range of 0 to 12, where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Months 6, 18, 30 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Month 6	59	67		
Month 18	42	50		
Month 30	41	48		
Month 42	26	28		

Statistical analyses

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	22

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	26.4

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID
Statistical analysis description:	
Month 30: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.	
Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	25.2

Statistical analysis title	Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

Comparison groups	Tofacitinib 5 mg BID v Tofacitinib 10 mg BID
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted (weighted) difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	18.5

Secondary: Change From Baseline in Fecal Calprotectin at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Change From Baseline in Fecal Calprotectin at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Change from baseline in fecal calprotectin (in micrograms per gram [mcg/g]) was reported. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	67		
Units: Micrograms per gram				
arithmetic mean (standard deviation)				
Change at Month 1 (n= 63, 62)	-137.5 (± 980.6)	-21.9 (± 304.7)		
Change at Month 3 (n= 57, 63)	-45.3 (± 1075.8)	-38.5 (± 313.6)		
Change at Month 6 (n= 52, 67)	-24.1 (± 1444.6)	-47.3 (± 331.4)		
Change at Month 9 (n= 48, 62)	-173.5 (± 1106.5)	-59.3 (± 380.8)		
Change at Month 12 (n= 46, 54)	-28.8 (± 1113.4)	-45.0 (± 350.7)		
Change at Month 15 (n= 45, 49)	-104.8 (± 1210.2)	69.3 (± 480.5)		
Change at Month 18 (n= 39, 44)	-51.0 (± 1114.6)	6.6 (± 565.4)		
Change at Month 21 (n= 43, 46)	-71.0 (± 1254.6)	-29.3 (± 462.7)		

Change at Month 24 (n= 41, 43)	118.3 (± 1591.4)	-69.8 (± 407.0)		
Change at Month 27 (n= 38, 39)	87.3 (± 478.8)	-49.1 (± 366.3)		
Change at Month 30 (n= 36, 40)	-8.5 (± 458.5)	-8.9 (± 518.5)		
Change at Month 33 (n= 36,38)	84.4 (± 434.5)	-4.9 (± 484.8)		
Change at Month 36 (n= 38, 36)	230.7 (± 1162.5)	-0.4 (± 449.4)		
Change at Month 39 (n= 28, 26)	-116.2 (± 472.8)	-98.3 (± 532.9)		
Change at Month 42 (n= 24, 23)	-44.7 (± 278.9)	-101.0 (± 452.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in High Sensitivity C-Reactive Protein (hs-CRP) Level at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point title	Change From Baseline in High Sensitivity C-Reactive Protein (hs-CRP) Level at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point description:

Change From baseline in hs-CRP level (in milligrams per liter [mg/L]) was reported. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point.

End point type	Secondary

End point timeframe:

Baseline, Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	67		
Units: Milligrams per liter				
arithmetic mean (standard deviation)				
Change at Month 1 (n= 63, 67)	1.1 (± 9.8)	-0.7 (± 3.4)		
Change at Month 3 (n= 56, 66)	0.7 (± 7.9)	-0.2 (± 3.7)		
Change at Month 6 (n= 55, 66)	0.9 (± 5.8)	0.1 (± 4.0)		
Change at Month 9 (n= 50, 63)	0.7 (± 11.1)	1.1 (± 8.4)		
Change at Month 12 (n= 48, 59)	-0.3 (± 3.5)	-0.2 (± 2.2)		
Change at Month 15 (n= 46, 51)	-0.7 (± 3.2)	0.2 (± 2.4)		
Change at Month 18 (n= 43, 48)	1.0 (± 6.4)	0.2 (± 1.9)		
Change at Month 21 (n= 44, 49)	-0.5 (± 3.3)	-0.1 (± 1.4)		
Change at Month 24 (n= 40, 43)	-0.6 (± 3.0)	-0.5 (± 2.2)		
Change at Month 27 (n= 39, 42)	-0.3 (± 2.8)	0.7 (± 6.1)		
Change at Month 30 (n= 39, 44)	0.6 (± 4.1)	-0.3 (± 1.9)		
Change at Month 33 (n= 38, 39)	0.1 (± 2.2)	0.0 (± 3.9)		
Change at Month 36 (n= 38, 36)	-0.1 (± 3.1)	-0.1 (± 3.9)		
Change at Month 39 (n= 37, 34)	-0.3 (± 3.5)	2.8 (± 8.6)		

Change at Month 42 (n= 27, 25)	0.6 (± 3.7)	5.9 (± 28.1)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; medically important events. A treatment emergent AE (TEAE) was defined as an event that emerged during the treatment period that was absent before treatment or worsened during the treatment period relative to the pretreatment state. AEs included both serious and all non-serious adverse events (irrespective of frequency threshold used to report other AEs in safety section). Safety analysis set (SAS) included all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
TEAEs	55	58		
SAEs	7	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Infections

End point title	Number of Subjects With Serious Infections

End point description:

Serious infections were defined as any infections (viral, bacterial, and fungal) requiring parenteral antimicrobial therapy, hospitalisation for treatment, or meeting other criteria that require the infection to be classified as serious adverse event. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; medically important events. SAS included all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Laboratory Abnormalities

End point title	Number of Subjects With Clinical Laboratory Abnormalities

End point description:

Abnormality criteria: Haematology: haemoglobin(Hg):<0.8* lower limit of normal(LLN); haematocrit:<0.8*LLN; lymphocytes:<0.8*LLN; lymphocytes/leukocytes: <0.8*LLN; erythrocytes(ery.):<0.8*LLN; ery. mean corpuscular volume: <0.9*LLN; ery. mean corpuscular Hg: <0.9*LLN; reticulocytes, reticulocytes/ery.:>1.5*upper limit of normal(ULN); neutrophils, neutrophils/leukocytes: >1.2*ULN; basophils/leukocytes, eosinophils, eosinophils/leukocytes, monocytes/leukocytes: >1.2*ULN; leukocyte esterase: >=1; Clinical chemistry: bicarbonate:<0.9*LLN, bilirubin(bil): >1.5*ULN; indirect bil: >1.5*ULN; aspartate aminotransferase(AT): >3.0*ULN; alanine AT: >3.0*ULN; gamma glutamyl transferase: >3.0*ULN; creatine kinase: >2.0*ULN; potassium: >1.1*ULN; blood urea nitrogen: >1.3*ULN; creatinine: >1.3*ULN; urate: >1.2*ULN; cholesterol: >1.3*ULN; HDL-cholesterol: <0.8*LLN; LDL-cholesterol: >1.2*ULN; triglycerides: >1.3*ULN; glucose: >1.5*ULN; urine Hg:>=1. SAS:all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 27 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects	33	51		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Laboratory Abnormalities Leading to Study Treatment Discontinuation

End point title	Number of Subjects With Clinically Significant Laboratory

	Abnormalities Leading to Study Treatment Discontinuation

End point description:

Laboratory abnormalities leading to study treatment discontinuation: 2 sequential neutrophil counts <750 neutrophils per cubic millimeter (mm^3); 2 sequential lymphocyte counts <500 lymphocytes/mm^3; 2 sequential hemoglobin <8.0 grams per deciliter; 2 sequential platelet counts <75000 platelets/mm^3; 2 sequential AST or ALT elevations >=3*ULN with at least one total bilirubin value >=2*ULN; 2 sequential AST or ALT elevations >=3*ULN accompanied by signs or symptoms consistent with hepatic injury; 2 sequential AST or ALT elevations >=5*ULN; 2 sequential increases in creatinine >50% and >0.5 milligrams per deciliter over A3921139 baseline; 2 sequential CK elevations >10*ULN unless the causality is known not to be medically serious (eg, exercise induced). SAS: all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Sign Abnormalities

End point title	Number of Subjects With Vital Sign Abnormalities

End point description:

Vital signs abnormality criteria included: 1) a) diastolic blood pressure (DBP) of (less than) <50 millimeter of mercury (mmHg), b) change greater than or equal to (>=) 20 mmHg increase, c) change >=20 mmHg decrease; 2) a) systolic blood pressure (SBP) of <90 mmHg, b) change >=30 mmHg increase, c) change >=30 mmHg decrease; 3) a) pulse rate value of <40 beats per minute (bpm), b) pulse rate >120 bpm. SAS included all subjects who received at least 1 dose of IP. Only those categories in which at least 1 subject had data were reported.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
DBP: <50 mmHg	3	0		
DBP: Change >= 20mmHg increase	9	5		
DBP: Change >= 20mmHg decrease	7	7		
SBP: <90mmHg	2	0		
SBP: Change >= 30mmHg increase	7	4		

SBP: Change >= 30mmHg decrease	6	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Physical Examinations Abnormalities

End point title	Number of Subjects With Clinically Significant Physical Examinations Abnormalities

End point description:

Physical examination included assessment of the weight, general appearance, eyes, mouth, lungs, heart, abdomen, musculoskeletal, extremities, skin and lymph nodes. Clinical significance was assessed by the investigator. SAS included all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects	28	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Opportunistic Infections, all Malignancy, Gastrointestinal Perforation and Cardiovascular Events Adjudicated by Adjudication Committee

End point title	Number of Subjects With Opportunistic Infections, all Malignancy, Gastrointestinal Perforation and Cardiovascular Events Adjudicated by Adjudication Committee

End point description:

Number of subjects with adjudicated opportunistic infections including herpes zoster (non-adjacent or >2 adjacent dermatomes); all malignancies including non-melanoma skin cancer; gastrointestinal perforation and cardiovascular events including pulmonary embolism and cerebrovascular accident, adjudicated by adjudication committee were reported. SAS included all subjects who received at least 1 dose of IP.

End point type	Secondary

End point timeframe:

Baseline up to 43 months

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	70		
Units: Subjects				
Opportunistic Infections	0	1		
All Malignancy	4	3		
Gastrointestinal Perforation	0	0		
Cardiovascular Events	2	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 43 months

Adverse event reporting additional description:

Same event may appear as AE and serious AE, what is presented are distinct events. Event may be categorised as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis set: all subjects who received at least 1 dose of investigational product.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Tofacitinib 10 mg BID

Reporting group description:

Subjects received tofacitinib 10 mg tablets (2 tablets of 5 mg), orally, twice daily up to 42 months. Subjects were followed-up to 4 weeks after the last dose.

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

Subjects received tofacitinib 5 mg tablet with one tablet of matching placebo, orally, twice daily up to 42 months. Subjects were followed up to 4 weeks after the last dose.

Serious adverse events	Tofacitinib 10 mg BID	Tofacitinib 5 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 70 (22.86%)	7 / 70 (10.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast disorder			

subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colon dysplasia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			

subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tofacitinib 10 mg BID	Tofacitinib 5 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 70 (67.14%)	47 / 70 (67.14%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 70 (7.14%)	4 / 70 (5.71%)	
occurrences (all)	5	4	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 70 (2.86%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Chest pain			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	2 / 70 (2.86%)	5 / 70 (7.14%)	
occurrences (all)	3	5	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Respiratory disorder			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Cough			

subjects affected / exposed	1 / 70 (1.43%)	3 / 70 (4.29%)	
occurrences (all)	2	3	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	3 / 70 (4.29%)	1 / 70 (1.43%)	
occurrences (all)	3	1	
Faecal calprotectin increased			
subjects affected / exposed	3 / 70 (4.29%)	1 / 70 (1.43%)	
occurrences (all)	3	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 70 (7.14%)	2 / 70 (2.86%)	
occurrences (all)	9	2	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 70 (4.29%)	0 / 70 (0.00%)	
occurrences (all)	5	0	
SARS-CoV-2 test positive			
subjects affected / exposed	7 / 70 (10.00%)	2 / 70 (2.86%)	
occurrences (all)	7	2	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 70 (4.29%)	4 / 70 (5.71%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 70 (4.29%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Lymphopenia			
subjects affected / exposed	5 / 70 (7.14%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Gastrointestinal disorders			
Colitis ulcerative			

subjects affected / exposed	14 / 70 (20.00%)	16 / 70 (22.86%)	
occurrences (all)	17	16	
Large intestine polyp			
subjects affected / exposed	3 / 70 (4.29%)	1 / 70 (1.43%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	3 / 70 (4.29%)	5 / 70 (7.14%)	
occurrences (all)	5	8	
Nausea			
subjects affected / exposed	3 / 70 (4.29%)	3 / 70 (4.29%)	
occurrences (all)	3	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	2 / 70 (2.86%)	4 / 70 (5.71%)	
occurrences (all)	2	4	
Abdominal pain upper			
subjects affected / exposed	2 / 70 (2.86%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Haemorrhoids			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 70 (0.00%)	3 / 70 (4.29%)	
occurrences (all)	0	3	
Mouth ulceration			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	1	

Rash pruritic			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 70 (2.86%)	4 / 70 (5.71%)	
occurrences (all)	2	4	
Arthritis			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Arthralgia			
subjects affected / exposed	5 / 70 (7.14%)	4 / 70 (5.71%)	
occurrences (all)	5	6	
Back pain			
subjects affected / exposed	2 / 70 (2.86%)	3 / 70 (4.29%)	
occurrences (all)	2	4	
Neck pain			
subjects affected / exposed	2 / 70 (2.86%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Osteoarthritis			
subjects affected / exposed	2 / 70 (2.86%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 70 (7.14%)	1 / 70 (1.43%)	
occurrences (all)	5	1	
Herpes zoster			
subjects affected / exposed	5 / 70 (7.14%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Influenza			
subjects affected / exposed	3 / 70 (4.29%)	1 / 70 (1.43%)	
occurrences (all)	3	2	

Oral herpes			
subjects affected / exposed	0 / 70 (0.00%)	5 / 70 (7.14%)	
occurrences (all)	0	8	
Nasopharyngitis			
subjects affected / exposed	8 / 70 (11.43%)	7 / 70 (10.00%)	
occurrences (all)	14	11	
Upper respiratory tract infection			
subjects affected / exposed	4 / 70 (5.71%)	3 / 70 (4.29%)	
occurrences (all)	5	5	
COVID-19			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Clostridium difficile infection			
subjects affected / exposed	0 / 70 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Sinusitis			
subjects affected / exposed	1 / 70 (1.43%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	1 / 70 (1.43%)	2 / 70 (2.86%)	
occurrences (all)	1	4	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 70 (1.43%)	2 / 70 (2.86%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2018	Protocol summary and section 3, study design were revised to change treatment duration from 18 months to 42 months. The purpose of this change was to gather additional long term safety data and to provide a longer time horizon to observe any potential divergence of efficacy between the two dose groups. Protocol summary, section 3, study design and section 9.1 sample size determination were revised to clarify that the final sample size may exceed 130 subjects. The purpose of this revision was to optimize recruitment of potentially eligible subjects from Study A3921139.
19 June 2019	As a result of the restrictions for prescriptions of tofacitinib set forth on 17 May 2019 by the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) in the European Union, a global amendment was incorporated. Subjects who were identified as having one or more of the contraindicated risk factors for pulmonary embolism as described by PRAC had their tofacitinib dose adjusted to open label 5 mg BID. Furthermore, any subject identified as having one or more of the contraindicated risk factors for pulmonary embolism as described by PRAC was not permitted to receive tofacitinib 10 mg BID. A risk factor check for pulmonary embolism was added for all study visits.
11 May 2020	As a result of the Sponsor determining that venous thromboembolism is an important identified risk/dose dependent adverse drug reaction for tofacitinib, a further global amendment regarding the monitoring and discontinuation guidelines for venous thromboembolism was incorporated. The changes described in the Protocol Administrative Clarification Letter for Amendment 2 due to COVID-19 were incorporated in the newly added Appendix 9.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 March 2022	The study terminated early due to business reasons, with the study already meeting its primary objective. The decision to terminate the trial was not based on any safety and/or efficacy concerns.	-

Notes:

Limitations and caveats

None reported