Clinical trial results:
A Multicentre, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Of Oral CP-690,550 As A Maintenance Therapy In Subjects With Ulcerative Colitis

Summary

EudraCT number	2011-004580-79
Trial protocol	DK CZ HU EE GB LV BE ES AT DE PL IT SK HR
Global end of trial date	27 May 2016

Results information

Result version number	v1 (current)
This version publication date	23 April 2017
First version publication date	23 April 2017

Trial information

Trial identification

Sponsor protocol code	A3921096

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01458574
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 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate the efficacy of tofacitinib as maintenance therapy in subjects with ulcerative colitis (UC).
2) To evaluate the safety and tolerability of tofacitinib as maintenance therapy in subjects with UC.
3) To evaluate the efficacy of tofacitinib maintenance therapy in achieving mucosal healing in subjects with UC.
4) To evaluate the tofacitinib pharmacokinetic exposure during maintenance therapy in subjects with UC.
5) To evaluate the effect of tofacitinib as maintenance therapy on quality-of-life in subjects with UC.

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 July 2012
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	Austria: 13
Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Poland: 40

Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Serbia: 20
Country: Number of subjects enrolled	Slovakia: 26
Country: Number of subjects enrolled	Ukraine: 39
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	United States: 114
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Japan: 39
Country: Number of subjects enrolled	Korea, Republic of: 23
Country: Number of subjects enrolled	New Zealand: 17
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	South Africa: 22
Worldwide total number of subjects	593
EEA total number of subjects	261

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)	545
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study subjects were enrolled from 196 investigational sites in Asia, Australia, Europe, North America, and South America. Overall, 593 subjects were randomized to study treatment. Study was conducted between 20 July 2012 and 27 May 2016.

Period 1

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

Arms

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

Arm description:

Subjects received tofacitinib 5 milligram (mg) tablets, orally, twice daily (BID) for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

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:

Tofacitinib 5 mg tablets, orally, BID for 53 weeks of double blind treatment period.

Arm title	Tofacitinib 10 mg BID

Arm description:

Subjects received tofacitinib 10 mg tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

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:

Tofacitinib 10 mg tablets, orally, BID for 53 weeks of double blind treatment period.

Arm title	Placebo

Arm description:

Subjects received tofacitinib matched placebo tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

Arm type	Placebo

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

Dosage and administration details:

Tofacitinib matched Placebo, orally, BID for 53 weeks of double blind treatment period.

Number of subjects in period 1	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo
Started	198	197	198
Treated	198	196	198
Completed	111	126	53
Not completed	87	71	145
Consent withdrawn by subject	6	3	5
Adverse event, non-fatal	5	9	7
Randomized but not treated	-	1	-
Pregnancy	1	1	-
Unspecified	2	1	-
Lost to follow-up	3	2	1
Lack of efficacy	70	53	132
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 milligram (mg) tablets, orally, twice daily (BID) for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	
Reporting group title	Placebo
Reporting group description:	
Subjects received tofacitinib matched placebo tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	

Reporting group values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo
Number of subjects	198	197	198
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age <37 weeks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	185	180	180
Adults (65-84 years)	13	17	18
Adults (85 years and over)	0	0	0
Age Continuous Units: years			
arithmetic mean	41.9	42.9	43.4
standard deviation	± 13.7	± 14.4	± 14
Gender, Male/Female Units: Subjects			
Female	95	87	82
Male	103	110	116

Reporting group values	Total		
Number of subjects	593		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age <37 weeks)	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)	545		
Adults (65-84 years)	48		
Adults (85 years and over)	0		
Age Continuous Units: years arithmetic mean standard deviation	 -		
Gender, Male/Female Units: Subjects			
Female	264		
Male	329		

End points

End points reporting groups

Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Subjects received tofacitinib 5 milligram (mg) tablets, orally, twice daily (BID) for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Subjects received tofacitinib 10 mg tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	
Reporting group title	Placebo
Reporting group description:	
Subjects received tofacitinib matched placebo tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.	

Primary: Percentage of Subjects in Remission at Week 52

End point title	Percentage of Subjects in Remission at Week 52
End point description:	
Remission in subjects 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 was an instrument designed to measure disease activity of ulcerative colitis (UC). It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and physician global assessment (PGA), each subscore graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12 where higher score indicating higher disease severity. Full analysis set (FAS) included all randomized subjects.	
End point type	Primary
End point timeframe:	
Week 52	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	34.3	40.6	11.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description:	
P-value based on Cochran-Mantel-Haenszel (CMH) chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95 percent (%) confidence interval (CI) based on normal approximation for the difference in binomial proportions. Missing data were imputed using Non-responder imputation (NRI).	
Comparison groups	Tofacitinib 5 mg BID v Placebo

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.3
upper limit	31.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	29.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.4
upper limit	37.6

Secondary: Percentage of Subjects With Mucosal Healing at Week 52

End point title	Percentage of Subjects With Mucosal Healing at Week 52

End point description:

Mucosal healing in subjects was defined by 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 subscores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	37.4	45.7	13.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	16
upper limit	32.5

Statistical analysis title	Tofacitinib 10 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	32.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.2
upper limit	41

Secondary: Percentage of Subjects in Sustained Steroid-Free Remission (Defined as Being in Remission and Steroid-Free at Both Week 24 and 52), Among Subjects With Remission at Baseline

End point title	Percentage of Subjects in Sustained Steroid-Free Remission (Defined as Being in Remission and Steroid-Free at Both Week 24 and 52), Among Subjects With Remission at Baseline

End point description:

Sustained steroid-free remission was defined by being in remission and steroid-free at both Week 24 and Week 52. Steroid-free remission was defined by being in remission, in addition to no requirement of any treatment with steroid for at least 4 weeks prior to the visit. Remission 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	55	59	
Units: percentage of subjects				
number (not applicable)	35.4	47.3	5.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	30.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	17.4
upper limit	43.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	42.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.9
upper limit	56.5

Secondary: Percentage of Subjects in Remission at Week 24

End point title	Percentage of Subjects in Remission at Week 24

End point description:

Remission in subjects 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher subscores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	33.8	35.5	11.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	22.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.8
upper limit	30.6

Statistical analysis title	Tofacitinib 10 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.4
upper limit	32.4

Secondary: Percentage of Subjects in Sustained Remission

End point title	Percentage of Subjects in Sustained Remission

End point description:

Sustained remission in subjects was defined by being in remission at both Week 24 and Week 52. Remission 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher subscores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher score indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	22.2	25.4	5.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.6
upper limit	23.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo

Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.5
upper limit	27.1

Secondary: Percentage of Subjects With Mucosal Healing at Week 24

End point title	Percentage of Subjects With Mucosal Healing at Week 24

End point description:

Mucosal healing in subjects was defined by a 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 indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	43.9	46.2	17.2	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	26.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	18.1
upper limit	35.5

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	29
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.3
upper limit	37.7

Secondary: Percentage of Subjects With Sustained Mucosal Healing

End point title	Percentage of Subjects With Sustained Mucosal Healing

End point description:

Sustained mucosal healing in subjects was defined by achieving mayo endoscopic subscore of 0 or 1 at both Week 24 and Week 52. The mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	27.8	33	6.6	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	21.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.1
upper limit	28.3

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	26.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	19
upper limit	33.8

Secondary: Percentage of Subjects With Mucosal Healing at Week 24 and 52, Among Subjects With Mucosal Healing at Baseline

End point title	Percentage of Subjects With Mucosal Healing at Week 24 and 52, Among Subjects With Mucosal Healing at Baseline

End point description:

Mucosal healing in subjects was defined as achieving 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 indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	89	101	
Units: percentage of subjects				
number (not applicable)				
Week 24	52.4	66.3	21.8	
Week 52	41.9	55.1	11.9	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	30.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.1
upper limit	43.1

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo

Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	44.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.8
upper limit	57.2

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.7
upper limit	41.4

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	43.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	31.1
upper limit	55.3

Secondary: Percentage of Subjects With Sustained Mucosal Healing, Among Subjects With Mucosal Healing at Baseline

End point title	Percentage of Subjects With Sustained Mucosal Healing, Among Subjects With Mucosal Healing at Baseline

End point description:

Sustained mucosal healing in subjects was defined by achieving mayo endoscopic subscore of 0 or 1 at both Week 24 and Week 52. The mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher scores indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	89	101	
Units: percentage of subjects				
number (not applicable)	33.3	49.4	8.9	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	24.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	35

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	40.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.7
upper limit	52.3

Secondary: Percentage of Subjects With Clinical Response at Week 24 and 52

End point title	Percentage of Subjects With Clinical Response at Week 24 and 52

End point description:

Clinical response was defined by a decrease from induction study (A3921094 [NCT01465763] or A3921095 [NCT01458951]) baseline in Mayo score of at least 3 points and at least 30%, 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. Percentage of subjects with clinical response at Week 24 and 52 have been reported in this endpoint. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)				
Week 24	63.6	70.6	33.3	
Week 52	51.5	61.9	20.2	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	30.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.9
upper limit	39.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	37.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.1
upper limit	46.4

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	31.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.4
upper limit	40.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	41.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.9
upper limit	50.5

Secondary: Percentage of Subjects With Sustained Clinical Response

End point title	Percentage of Subjects With Sustained Clinical Response

End point description:

Sustained clinical response in subjects was defined as showing clinical response at both Week 24 and Week 52. Clinical response was defined by a decrease from induction study (A3921094 [NCT01465763] or A3921095 [NCT01458951]) baseline in mayo score of at least 3 points and at least 30%, 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. Percentage of subjects with sustained clinical response are reported in this endpoint. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	49	59.4	19.2	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	29.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.9
upper limit	38.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo

Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	40.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.4
upper limit	49

Secondary: Percentage of Subjects in Clinical Remission at Week 24 and 52

End point title	Percentage of Subjects in Clinical Remission at Week 24 and 52

End point description:

Clinical remission in subjects was defined as a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)				
Week 24	34.3	35.5	11.1	
Week 52	34.3	41.1	11.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.3
upper limit	31.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.4
upper limit	32.4

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	23.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	15.3
upper limit	31.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.9
upper limit	38.2

Secondary: Percentage of Subjects in Sustained Clinical Remission

End point title	Percentage of Subjects in Sustained Clinical Remission

End point description:

Sustained clinical remission in subjects was defined as being in clinical remission at both Week 24 and Week 52. Clinical remission was defined by a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	22.2	25.9	5.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.6
upper limit	23.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo
Statistical analysis description:	
P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.	
Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	20.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	27.7

Secondary: Percentage of Subjects in Deep Remission at Week 24 and 52

End point title	Percentage of Subjects in Deep Remission at Week 24 and 52

End point description:

Deep remission in subjects was defined as a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point and 0 subscore for both rectal bleeding and endoscopic subscores. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)				
Week 24	14.1	10.7	4	
Week 52	14.6	15.2	4	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	15.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in

binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0092
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	11.7

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	16.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	11.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.5
upper limit	16.9

Secondary: Percentage of Subjects in Sustained Deep Remission

End point title	Percentage of Subjects in Sustained Deep Remission

End point description:

Sustained deep remission was defined by being in deep remission at both Week 24 and Week 52. Deep remission in subjects was defined as a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point and 0 subscore for both rectal bleeding and endoscopic subscores. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	6.1	3.6	0.5	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	5.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	9

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	5.8

Secondary: Percentage of Subjects in Symptomatic Remission at Week 24 and 52

End point title	Percentage of Subjects in Symptomatic Remission at Week 24 and 52

End point description:

Symptomatic remission in subjects was defined as a total mayo score of 2 points or lower, with no individual subscore exceeding 1 point, and 0 subscore for both rectal bleeding and stool frequency. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 sub-scores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)				
Week 24	23.7	21.8	6.6	
Week 52	22.7	26.9	7.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.3
upper limit	24

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	15.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.5
upper limit	22

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.8
upper limit	22.5

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	19.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.7
upper limit	27

Secondary: Percentage of Subjects in Sustained Symptomatic Remission

End point title	Percentage of Subjects in Sustained Symptomatic Remission

End point description:

Sustained symptomatic remission in subjects was defined as being in symptomatic remission at both Week 24 and Week 52. Symptomatic remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point, and 0 subscore for both rectal bleeding and stool frequency. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4

subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	13.6	15.7	2.5	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.9
upper limit	16.4

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo

Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	18.7

Secondary: Percentage of Subjects in Endoscopic Remission at Week 24 and 52

End point title	Percentage of Subjects in Endoscopic Remission at Week 24 and 52

End point description:

Endoscopic remission in subjects was defined as a mayo endoscopic subscore of 0. The mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher subscores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)				
Week 24	16.2	12.2	4	
Week 52	14.6	16.8	4	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.3
upper limit	17.9

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	13.5

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	10.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	16.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.8
upper limit	18.6

Secondary: Percentage of Subjects in Sustained Endoscopic Remission

End point title	Percentage of Subjects in Sustained Endoscopic Remission

End point description:

Sustained endoscopic remission in subjects was defined as being in endoscopic remission at both Week 24 and Week 52. Endoscopic remission was defined by a mayo endoscopic subscore of 0. The mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher subscores indicating higher disease severity. FAS included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: percentage of subjects				
number (not applicable)	6.1	5.1	0.5	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	9

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	7.8

Secondary: Total Mayo Score at Baseline, Week 24 and 52

End point title	Total Mayo Score at Baseline, Week 24 and 52

End point description:

Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects. Here "n" signifies those subjects who were evaluable for specified categories, respectively.

End point type	Secondary
End point timeframe: Baseline, Week 24, 52	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 198, 197, 198)	3.3 (± 1.8)	3.4 (± 1.8)	3.3 (± 1.8)	
Week 24 (n = 179, 186, 181)	4.1 (± 3.4)	4 (± 3.3)	6.7 (± 3.5)	
Week 52 (n = 129, 137, 68)	3.2 (± 3.1)	2.6 (± 2.7)	4.6 (± 3.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Mayo Score at Week 24 and 52

End point title	Change from Baseline in Total Mayo Score at Week 24 and 52
End point description: Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. Change from baseline in total mayo score at Week 24 and 52 was reported. FAS included all randomized subjects. Here "n" signifies those subjects who were evaluable for specified categories, respectively.	
End point type	Secondary
End point timeframe: Baseline, Week 24, 52	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	197	198	
Units: units on a scale				
least squares mean (standard error)				
Change at Week 24 (n = 179, 186, 181)	0.3 (± 0.3)	0 (± 0.3)	2.9 (± 0.3)	
Change at Week 52 (n = 129, 137, 68)	0.4 (± 0.3)	-0.4 (± 0.3)	2.9 (± 0.4)	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description: At Week 24	
Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Linear mixed effect model
Parameter estimate	Least Square Mean Difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	-1.9

Statistical analysis title	Tofacitinib 10 mg BID, Placebo
Statistical analysis description: At Week 24	
Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Linear mixed effect model
Parameter estimate	Least Square Mean Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	-2.2

Statistical analysis title	Tofacitinib 5 mg BID, Placebo
Statistical analysis description: At Week 52	
Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Linear mixed effect model
Parameter estimate	Least Square Mean Difference
Point estimate	-2.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-1.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo
Statistical analysis description:	
At Week 52	
Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	395
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Linear mixed effect model
Parameter estimate	Least Square Mean Difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	-2.5

Secondary: Percentage of Subjects in Remission, Among Subjects With Remission at Baseline

End point title	Percentage of Subjects in Remission, Among Subjects With Remission at Baseline

End point description:

Remission in subjects 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher score indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	55	59	
Units: percentage of subjects				
number (not applicable)				
Week 24	55.4	63.6	15.3	

Week 52	46.2	56.4	10.2	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	25
upper limit	55.3

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	48.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.7
upper limit	64.1

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	36
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.6
upper limit	50.3

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	46.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	31
upper limit	61.4

Secondary: Percentage of Subjects in Sustained Remission, Among Subjects With Remission at Baseline

End point title	Percentage of Subjects in Sustained Remission, Among Subjects With Remission at Baseline

End point description:

Sustained remission in subjects was defined by being in remission at both Week 24 and Week 52. Remission was defined as 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher score indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	55	59	
Units: percentage of subjects				
number (not applicable)	36.9	47.3	5.1	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	31.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.8
upper limit	44.8

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	42.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	27.9
upper limit	56.5

Secondary: Percentage of Subjects in Steroid-free Remission, Among Subjects in Remission at Baseline

End point title	Percentage of Subjects in Steroid-free Remission, Among Subjects in Remission at Baseline

End point description:

Steroid-free remission was defined by being in remission, in addition to no requirement of any treatment with steroid for at least 4 weeks prior to the visit. Remission 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. Percentage of subjects in steroid-free remission were reported in this endpoint. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	55	59	
Units: percentage of subjects				
number (not applicable)				
Week 24	53.8	63.6	15.3	
Week 52	44.6	56.4	10.2	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	38.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.4
upper limit	53.8

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	48.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.7
upper limit	64.1

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	34.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	20.1
upper limit	48.8

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	46.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	31
upper limit	61.4

Secondary: Percentage of Subjects in Steroid-Free Remission, Among Subjects Receiving Steroids at Baseline

End point title	Percentage of Subjects in Steroid-Free Remission, Among Subjects Receiving Steroids at Baseline

End point description:

Steroid-free remission was defined by being in remission, in addition to no requirement of any treatment with steroid for at least 4 weeks prior to the visit. Remission 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. Percentage of subjects in steroid-free remission were reported in this endpoint. FAS included all randomized subjects. Here "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	87	101	
Units: percentage of subjects				
number (not applicable)				
Week 24	23.8	24.1	10.9	
Week 52	27.7	27.6	10.9	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0074
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	23.2

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 24: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0103
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	24.1

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0018
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	16.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.2
upper limit	27.5

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

At Week 52: P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.5
upper limit	27.9

Secondary: Percentage of Subjects in Sustained Steroid-Free Remission, Among Subjects Receiving Steroids at Baseline

End point title	Percentage of Subjects in Sustained Steroid-Free Remission, Among Subjects Receiving Steroids at Baseline

End point description:

Sustained steroid-free remission was defined by being in remission and steroid-free at both Week 24 and Week 52. Steroid-free remission was defined by being in remission, in addition to no requirement of

any treatment with steroid for at least 4 weeks prior to the visit. Remission 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 was an instrument designed to measure disease activity of UC. It consisted of 4 subscores: stool frequency, rectal bleeding, findings of centrally read flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicating higher disease severity. These subscores were summed up to give a total score range of 0 to 12, where higher scores indicating higher disease severity. FAS included all randomized subjects. Here "number of subjects analyzed" signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24, 52

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	87	101	
Units: percentage of subjects				
number (not applicable)	12.9	16.1	5	

Statistical analyses

Statistical analysis title	Tofacitinib 5 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 5 mg BID v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0419
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	15.7

Statistical analysis title	Tofacitinib 10 mg BID, Placebo

Statistical analysis description:

P-value based on CMH chi-square test stratified by induction study treatment and baseline remission status. Difference and its 95% CI based on normal approximation for the difference in binomial proportions. Missing data were imputed using NRI.

Comparison groups	Tofacitinib 10 mg BID v Placebo

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0121
Method	CMH chi-square test
Parameter estimate	Difference in percentage
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	19.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 57

Adverse event reporting additional description:

Same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event. Safety analysis included all treated subjects.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

Subjects received tofacitinib 5 mg tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

Reporting group title	Placebo

Reporting group description:

Subjects received tofacitinib matched placebo tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

Reporting group title	Tofacitinib 10 mg BID

Reporting group description:

Subjects received tofacitinib 10 mg tablets, orally, BID for 53 weeks of double blind treatment period. Subjects were followed-up for 4 weeks if withdrew from study participation.

Serious adverse events	Tofacitinib 5 mg BID	Placebo	Tofacitinib 10 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 198 (5.05%)	13 / 198 (6.57%)	11 / 196 (5.61%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma	Additional description: This AE was gender specific.		
subjects affected / exposed[1]	0 / 95 (0.00%)	1 / 82 (1.22%)	0 / 86 (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

Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism venous			
subjects affected / exposed	0 / 198 (0.00%)	1 / 198 (0.51%)	0 / 196 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			

subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous	Additional description: This AE was gender specific.		
subjects affected / exposed[2]	1 / 95 (1.05%)	0 / 82 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 198 (0.00%)	1 / 198 (0.51%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			

subjects affected / exposed	2 / 198 (1.01%)	8 / 198 (4.04%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 198 (0.00%)	1 / 198 (0.51%)	0 / 196 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spondylolisthesis			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacterial diarrhoea			
subjects affected / exposed	0 / 198 (0.00%)	0 / 198 (0.00%)	1 / 196 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 198 (0.00%)	1 / 198 (0.51%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 198 (0.00%)	1 / 198 (0.51%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 198 (0.51%)	0 / 198 (0.00%)	0 / 196 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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: This AE was gender specific

[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: This AE was gender specific

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Tofacitinib 5 mg BID	Placebo	Tofacitinib 10 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 198 (43.94%)	108 / 198 (54.55%)	107 / 196 (54.59%)

Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	6 / 198 (3.03%)	4 / 198 (2.02%)	13 / 196 (6.63%)
occurrences (all)	8	4	16
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 198 (8.59%)	12 / 198 (6.06%)	6 / 196 (3.06%)
occurrences (all)	21	14	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 198 (4.04%)	11 / 198 (5.56%)	4 / 196 (2.04%)
occurrences (all)	8	12	4
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 198 (2.53%)	11 / 198 (5.56%)	7 / 196 (3.57%)
occurrences (all)	5	13	9
Colitis ulcerative			
subjects affected / exposed	35 / 198 (17.68%)	64 / 198 (32.32%)	29 / 196 (14.80%)
occurrences (all)	41	65	30
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 198 (3.03%)	8 / 198 (4.04%)	11 / 196 (5.61%)
occurrences (all)	6	8	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 198 (8.59%)	19 / 198 (9.60%)	17 / 196 (8.67%)
occurrences (all)	21	22	19
Infections and infestations			
Herpes zoster			
subjects affected / exposed	2 / 198 (1.01%)	1 / 198 (0.51%)	10 / 196 (5.10%)
occurrences (all)	2	1	11
Nasopharyngitis			
subjects affected / exposed	19 / 198 (9.60%)	11 / 198 (5.56%)	27 / 196 (13.78%)
occurrences (all)	21	23	39
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	13 / 198 (6.57%) 15	7 / 198 (3.54%) 8	12 / 196 (6.12%) 14
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	4 / 198 (2.02%) 5	2 / 198 (1.01%) 2	11 / 196 (5.61%) 11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2012	This amendment updated standard Pfizer protocol text, including safety language in various sections, including Administration, Reproductive Status of Female Subjects, and AE Reporting. In addition, this amendment included updates to the summary of safety section for tofacitinib to be consistent with the revised investigator's brochure (IB), secondary study endpoints, schedule of activities flowchart, and prohibited medication list. Guidelines and clarifications were included which provided instruction for dosage adjustment, temporary withholding of study drug, and scheduled study visit procedures.
20 April 2016	This administrative amendment clarified the multiple comparison procedure stated in Section 9.2.2 so that it guaranteed the control of the family-wise Type I error rate at 0.05.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported