Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Study to Investigate the Safety and Efficacy of CP-690,550 for Induction Therapy in Subjects with Moderate to Severe Crohn's Disease

Summary

EudraCT number	2011-001733-16
Trial protocol	DE SE ES HU GR AT CZ NL BG HR
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	26 March 2016
First version publication date	26 March 2016

Trial information

Trial identification

Sponsor protocol code	A3921083

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01393626
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	23 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This Phase 2b, randomised, double-blind, placebo-controlled, parallel group, dose-ranging, multicentre study evaluated subjects with moderate to severe active Crohn's disease. The primary objective of the study was to evaluate the dose-response of tofacitinib in inducing clinical remission in subjects with moderate to severe Crohn's disease and to select effective dose(s). Secondary objectives were to evaluate the safety and tolerability of tofacitinib induction therapy, to evaluate the dose-response of tofacitinib in inducing clinical response, to characterize the pharmacokinetics (PK) of tofacitinib, to evaluate the effect of tofacitinib on quality of life, and to evaluate the effect of tofacitinib on C-reactive protein (CRP) and fecal calprotectin, all in subjects with moderate to severe Crohn's disease.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2011
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	Australia: 10
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Korea, Republic of: 15
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 21

Country: Number of subjects enrolled	Ukraine: 10
Country: Number of subjects enrolled	United States: 103
Worldwide total number of subjects	279
EEA total number of subjects	99

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)	273
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening confirmed documented clinical diagnosis of Crohn’s disease (for at least 6 months prior), QuantiFERON® tuberculosis Gold test/chest radiograph, colonoscopy, magnetic resonance imaging & satisfactory laboratory, vital sign, physical examination & 12-lead electrocardiogram results within 1 to 3 weeks prior to Day 1.

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	Placebo

Arm description:

Placebo tablets to match tofacitinib 5 milligrams (mg) for oral administration twice daily (BID) for 8 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo for Tofacitinib (CP-690550)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets to match tofacitinib for oral administration BID for 8 weeks.

Arm title	Tofacitinib 5 mg BID

Arm description:

Tofacitinib tablets for oral administration at a dose of 5 mg BID for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib (CP-690550)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One 5 mg tofacitinib tablet for oral administration BID for 8 weeks.

Arm title	Tofacitinib 10 mg BID

Arm description:

Tofacitinib tablets for oral administration at a dose of 10 mg BID for 8 weeks.

Arm type	Experimental

Investigational medicinal product name	Tofacitinib (CP-690550)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Two 5 mg tofacitinib tablets for oral administration BID for 8 weeks.

Arm title	Tofacitinib 15 mg BID

Arm description:

Tofacitinib tablets for oral administration at a dose of 15 mg BID for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib (CP-690550)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Three 5 mg tofacitinib tablets for oral administration BID for 8 weeks.

Number of subjects in period 1	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Started	91	86	86
Completed	73	74	74
Not completed	18	12	12
Consent withdrawn by subject	6	4	-
Did not meet entrance criteria	1	-	-
Adverse event, non-fatal	2	1	5
Unspecified	1	-	-
Lost to follow-up	1	1	1
Lack of efficacy	6	6	4
Protocol deviation	1	-	2

Number of subjects in period 1	Tofacitinib 15 mg BID
Started	16
Completed	15
Not completed	1
Consent withdrawn by subject	-
Did not meet entrance criteria	-
Adverse event, non-fatal	-
Unspecified	-
Lost to follow-up	-
Lack of efficacy	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets to match tofacitinib 5 milligrams (mg) for oral administration twice daily (BID) for 8 weeks.	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 5 mg BID for 8 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 10 mg BID for 8 weeks.	
Reporting group title	Tofacitinib 15 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 15 mg BID for 8 weeks.	

Reporting group values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Number of subjects	91	86	86
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	91	85	82
From 65-84 years	0	1	4
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	37.2	40.2	39.3
standard deviation	± 11.7	± 11.5	± 13.7
Gender, Male/Female Units: Participants			
Female	60	32	47
Male	31	54	39

Reporting group values	Tofacitinib 15 mg BID	Total	
Number of subjects	16	279	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	273	
From 65-84 years	1	6	
85 years and over	0	0	
Age Continuous |			
Units: Years			
arithmetic mean	41.3		
standard deviation	± 14.3	-	
Gender, Male/Female			
Units: Participants			
Female	7	146	
Male	9	133	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo tablets to match tofacitinib 5 milligrams (mg) for oral administration twice daily (BID) for 8 weeks.	
Reporting group title	Tofacitinib 5 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 5 mg BID for 8 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 10 mg BID for 8 weeks.	
Reporting group title	Tofacitinib 15 mg BID
Reporting group description:	
Tofacitinib tablets for oral administration at a dose of 15 mg BID for 8 weeks.	

Primary: Percentage of Participants in Clinical Remission (as Defined by a Crohn's Disease Activity Index [CDAI] Score of Less Than [<] 150 Points) at Week 8

End point title	Percentage of Participants in Clinical Remission (as Defined by a Crohn's Disease Activity Index [CDAI] Score of Less Than [<] 150 Points) at Week 8[1]

End point description:

Clinical remission was a CDAI < 150 points. CDAI is a composite index consisting of a weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI score was based partly on entries (7 days before evaluation) from participant's diary kept while on study. CDAI scores range from 0 to approximately 600, higher score indicates higher disease activity.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Primary

End point timeframe:

Week 8

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	86	
Units: Percentage of Participants				
number (confidence interval 95%)	36.67 (26.75 to 47.49)	43.53 (32.8 to 54.72)	43.02 (32.39 to 54.15)	

Statistical analyses

Statistical analysis title	Analysis of Clinical Remission at Week 8
Statistical analysis description: Tofacitinib-Placebo	
Comparison groups	Placebo v Tofacitinib 5 mg BID
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3249
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	6.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.64
upper limit	21.36

Statistical analysis title	Analysis of Clinical Remission at Week 8
Statistical analysis description: Tofacitinib-Placebo	
Comparison groups	Placebo v Tofacitinib 10 mg BID
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3916
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	6.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.09
upper limit	20.8

Secondary: Percentage of Participants in Clinical Remission (CDAI <150) at Weeks 2 and 4

End point title	Percentage of Participants in Clinical Remission (CDAI <150) at Weeks 2 and 4[2]

End point description:

Clinical remission was a CDAI <150 points. CDAI is a composite index consisting of a weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI score was based partly on entries (7 days before evaluation) from participant's diary kept while on study. CDAI scores range from 0 to approximately 600, higher score indicates higher disease activity.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Weeks 2 and 4

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	86	
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 2	10 (4.68 to 18.14)	9.41 (4.15 to 17.71)	9.3 (4.1 to 17.51)	
Week 4	21.11 (13.21 to 30.99)	24.71 (15.99 to 35.25)	22.09 (13.86 to 32.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Response-70 (as Defined by a Decrease in CDAI Score of at Least 70 Points from Baseline) at Weeks 2, 4, and 8

End point title	Percentage of Participants Achieving Clinical Response-70 (as Defined by a Decrease in CDAI Score of at Least 70 Points from Baseline) at Weeks 2, 4, and 8[3]

End point description:

Clinical response-70 was defined as a reduction in CDAI score from baseline of at least 70 points. CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI scores range from 0 to approximately 600 points, higher score indicates higher disease activity.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and 8

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	86	
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 2	37.78 (27.77 to 48.62)	47.06 (36.13 to 58.19)	44.19 (33.48 to 55.3)	
Week 4	50 (39.27 to 60.73)	57.65 (46.45 to 68.3)	56.98 (45.85 to 67.61)	
Week 8	62.22 (51.38 to 72.23)	76.47 (66.03 to 85)	74.42 (63.87 to 83.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Response-100 (as Defined by a Decrease in CDAI Score of at Least 100 Points from Baseline) at Weeks 2, 4, and 8

End point title	Percentage of Participants Achieving Clinical Response-100 (as Defined by a Decrease in CDAI Score of at Least 100 Points from Baseline) at Weeks 2, 4, and 8[4]

End point description:

Clinical response-100 was defined as a reduction in CDAI score from baseline of at least 100 points. CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI scores range from 0 to approximately 600 points, higher score indicates higher disease activity.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and 8

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	86	
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 2	23.33 (15.06 to 33.43)	34.12 (24.18 to 45.2)	32.56 (22.84 to 43.52)	
Week 4	37.78 (27.77 to 48.62)	48.24 (37.26 to 59.34)	45.35 (34.58 to 56.45)	
Week 8	54.44 (43.6 to 64.98)	70.59 (59.71 to 79.98)	68.6 (57.7 to 78.19)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Either Clinical Response-100 or Clinical Remission (CDAI<150) at Weeks 2, 4, and 8

End point title	Percentage of Participants Achieving Either Clinical Response-100 or Clinical Remission (CDAI<150) at Weeks 2, 4, and 8[5]

End point description:

Clinical response-100 was defined as a reduction in CDAI score from baseline of at least 100 points. Clinical remission was a CDAI < 150 points. CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI scores range from 0 to approximately 600 points, higher score indicates higher disease activity.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, and 8

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	86	
Units: Percentage of Participants				
number (confidence interval 95%)				
Week 2	24.44 (16 to 34.64)	34.12 (24.18 to 45.2)	32.56 (22.84 to 43.52)	
Week 4	38.89 (28.79 to 49.74)	49.41 (38.39 to 60.48)	46.51 (35.68 to 57.59)	
Week 8	55.56 (44.7 to 66.04)	71.76 (60.96 to 81)	69.77 (58.92 to 79.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: CDAI Scores at Weeks 2, 4, and 8

End point title	CDAI Scores at Weeks 2, 4, and 8

End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, extent of abdominal pain, general well-being, occurrence of extra-intestinal symptoms, need for antidiarrheal drugs, presence of abdominal masses, hematocrit, and body weight. CDAI scores range from 0 to approximately 600 points, higher score indicates higher disease activity.

End point type	Secondary

End point timeframe:

Weeks 2, 4, and 8

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	85	86	16
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=85, 78, 77, 16)	258.04 (± 89.79)	237.6 (± 67.87)	241.21 (± 75.27)	270.31 (± 90.78)
Week 4 (n=81, 78, 71, 15)	228.65 (± 102.01)	213.38 (± 86.04)	203.58 (± 86.69)	228.27 (± 103.01)
Week 8 (n=80, 77, 75, 15)	194.9 (± 111.88)	162.77 (± 87.67)	159.08 (± 81.3)	172.47 (± 119.28)

Statistical analyses

No statistical analyses for this end point

Secondary: C-Reactive Protein (CRP) Serum Concentrations at Weeks 2, 4, and 8

End point title	C-Reactive Protein (CRP) Serum Concentrations at Weeks 2, 4, and 8

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement.

End point type	Secondary

End point timeframe:

Weeks 2, 4, and 8

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	85	86	16
Units: Milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 2 (n=89, 84, 81, 16)	17.28 (± 23.07)	8.26 (± 11.4)	8.56 (± 14.03)	7.89 (± 9.42)
Week 4 (n=83, 82, 78, 16)	18.94 (± 31.26)	8.17 (± 10.6)	9.48 (± 21.35)	10.33 (± 16.8)
Week 8 (n=80, 77, 74, 15)	18.12 (± 26.42)	9.49 (± 15.33)	6.55 (± 11)	5.77 (± 7.74)

Statistical analyses

No statistical analyses for this end point

Secondary: Calprotectin Fecal Concentrations at Weeks 2, 4, and 8

End point title	Calprotectin Fecal Concentrations at Weeks 2, 4, and 8

End point description:

Fecal calprotectin is an inflammatory marker for the gastrointestinal tract and considered as a measurement of neutrophil migration to the gastrointestinal tract. Higher values indicate more serious inflammation.

End point type	Secondary

End point timeframe:

Weeks 2, 4, and 8

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	85	86	16
Units: mg per kilogram (mg/kg)				
arithmetic mean (standard deviation)				
Week 2 (n=81, 76, 73, 16)	492.95 (± 664.51)	384.81 (± 342.9)	403.35 (± 352.57)	455.1 (± 461.87)
Week 4 (n=81, 82, 71, 16)	493.26 (± 682.81)	467.09 (± 377.65)	359.3 (± 306.88)	338.11 (± 391.65)
Week 8 (n=75, 66, 72, 14)	428.45 (± 479.36)	417.7 (± 336.75)	385.66 (± 316.71)	349.61 (± 365.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Tofacitinib Plasma Concentrations from 0 to 2 hours Post Dose on Day 1 and at Week 8/Early Termination (ET) Visit

End point title	Tofacitinib Plasma Concentrations from 0 to 2 hours Post Dose on Day 1 and at Week 8/Early Termination (ET) Visit[6]

End point description:

Plasma samples were collected from participants for the determination of tofacitinib concentrations. Only samples from tofacitinib-treated participants were subsequently analyzed. Plasma concentration data are summarized by nominal sample collection times specified in the protocol, and actual sample collection times may be different. 9999 indicates number of observations above the lower limit of quantification equals (=) 0.

End point type	Secondary

End point timeframe:

Pre-dose, 20 minutes, 40 minutes, 1 hour, and 2 to 3 hours post-dose on Day 1 and Week 8/ET visit

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants from "Tofacitinib" treatment arms were planned to be analysed for this end point.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	86	16	
Units: nanograms per milliliter				
arithmetic mean (standard deviation)				
Day 1, 0 hours (n=83, 83, 16)	0.006687 (± 0.049144)	1.193 (± 9.0312)	9999 (± 9999)	
Day 1, 20 minutes (n=82, 83, 16)	27.44 (± 27.335)	62.28 (± 60.795)	65.83 (± 63.232)	
Day 1, 40 minutes (n=82, 81, 16)	41.03 (± 24.21)	84.61 (± 47.47)	151.4 (± 61.288)	
Day 1, 1 hour (n=83, 83, 16)	41.22 (± 18.432)	82.48 (± 40.782)	149.9 (± 42.22)	
Day 1, 2 hours (n=83, 82, 16)	31.85 (± 12.442)	70.01 (± 24.838)	106.1 (± 26.661)	
Week 8/ET, 0 hours (n=78, 72, 13)	4.216 (± 7.1089)	11.57 (± 21.453)	23.89 (± 45.837)	
Week 8/ET, 20 minutes (n=70, 70, 12)	25.89 (± 21.485)	71.14 (± 54.969)	127.6 (± 89.861)	
Week 8/ET, 40 minutes (n=70, 69, 12)	37.75 (± 23.891)	93.09 (± 46.471)	148.7 (± 58.948)	
Week 8/ET, 1 hour (n=70, 69, 12)	37.47 (± 21.384)	83.14 (± 35.1)	144.7 (± 48.137)	
Week 8/ET, 2 hours (n=72, 70, 13)	27.61 (± 15.742)	62.38 (± 27.505)	92.03 (± 27.806)	

Statistical analyses

No statistical analyses for this end point

Secondary: Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score and Domain Scores (Bowel Function, Emotional Status, Systemic Symptoms, and Social Function) at Baseline and Week 8/ET Visit

End point title	Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score and Domain Scores (Bowel Function, Emotional Status, Systemic Symptoms, and Social Function) at Baseline and

	Week 8/ET Visit

End point description:

The IBDQ is a psychometrically validated patient reported outcome (PRO) instrument for measuring disease-specific quality of life (QOL) in participants with inflammatory bowel disease (IBD). IBDQ consists of 32 items, each item score ranged from 1 (worst possible response) to 7 (best possible response). Total score is the sum of each item score, and ranged from 32 to 224 with a higher score indicating a better QOL. Positive change in total score indicated improvement in QOL.
Number of Subjects Analysed is the number of participants with non-missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	84	81	16
Units: Score on a scale				
arithmetic mean (standard deviation)				
IBDQ Total Score, Baseline	118.5 (± 28.48)	117.89 (± 27.98)	113.67 (± 28.45)	124.19 (± 26.97)
IBDQ Total Score, Week 8/ET	144.99 (± 37.97)	159.14 (± 35.39)	156.64 (± 36.66)	159 (± 47.98)
Bowel Function Score, Baseline	37.78 (± 8.17)	37.39 (± 9.37)	36.29 (± 7.72)	37.5 (± 9.78)
Bowel Function Score, Week 8/ET	45.76 (± 12.19)	50.94 (± 11.02)	50.69 (± 11.02)	52.5 (± 13.81)
Emotional Status Score, Baseline	45.88 (± 13.04)	45.34 (± 13.27)	44.55 (± 13.27)	47.25 (± 10.41)
Emotional Status Score, Week 8/ET	56.31 (± 14.39)	59.54 (± 13.78)	58.32 (± 14.71)	57.25 (± 20.07)
Systemic Symptoms Score, Baseline	15.22 (± 5.24)	15.58 (± 4.36)	14.6 (± 4.78)	16.44 (± 5.35)
Systemic Symptoms Score, Week 8/ET	19.7 (± 6.51)	22.24 (± 6.3)	21.8 (± 6.27)	22.88 (± 7.05)
Social Function Score, Baseline	19.62 (± 7.28)	19.48 (± 6.62)	18.23 (± 7.09)	23 (± 6.29)
Social Function Score, Week 8/ET	23.23 (± 8.47)	26.43 (± 7.57)	25.83 (± 7.8)	26.38 (± 9.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline IBDQ Total Score and Domain Scores (Bowel Function, Emotional Status, Systemic Symptoms, and Social Function) at Week 8/ET Visit Using Analysis of Covariance (ANCOVA)

End point title	Change from Baseline IBDQ Total Score and Domain Scores (Bowel Function, Emotional Status, Systemic Symptoms, and Social Function) at Week 8/ET Visit Using Analysis of Covariance (ANCOVA)[7]

End point description:

The IBDQ is a psychometrically validated PRO instrument for measuring disease-specific QOL in participants with IBD. IBDQ consists of 32 items, each item score ranged from 1 (worst possible response) to 7 (best possible response). Total score is the sum of each item score, and ranged from 32 to 224 with a higher score indicating a better QOL. Positive change in total score indicated improvement in QOL. Adjusted means were derived from the ANCOVA model with baseline value as a covariate, treatment group and prior use of anti-tumor necrosis factor (TNF) alpha (α) treatments as factors.The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol

Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.
Number of Subjects Analysed is the maximum number of participants with non-missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	84[8]	81	
Units: Score on a scale				
arithmetic mean (standard error)				
IBDQ Total Score	26.58 (± 3.76)	41.2 (± 3.9)	40.05 (± 3.9)	
Bowel Function Score	8.36 (± 1.23)	13.76 (± 1.28)	13.88 (± 1.28)	
Emotional Status Score	10.33 (± 1.37)	13.87 (± 1.42)	12.54 (± 1.43)	
Systemic Symptoms Score	4.41 (± 0.66)	6.7 (± 0.69)	6.68 (± 0.69)	
Social Function Score	3.68 (± 0.79)	7.03 (± 0.82)	6.95 (± 0.82)	

Notes:

[8] - (Number of subjects analysed for Social Function Score = 83)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an IBDQ Total Score of Greater than or Equal to (≥) 170 at Week 8/ET Visit

End point title	Percentage of Participants with an IBDQ Total Score of Greater than or Equal to (≥) 170 at Week 8/ET Visit

End point description:

The IBDQ is a psychometrically validated PRO instrument for measuring disease-specific QOL in participants with IBD. IBDQ consists of 32 items, each item score ranged from 1 (worst possible response) to 7 (best possible response). Total score is the sum of each item score, and ranged from 32 to 224 with a higher score indicating a better QOL. Positive change in total score indicated improvement in QOL.

End point type	Secondary

End point timeframe:

Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	84	81	16
Units: Percentage of Participants				
number (not applicable)	26.1	45.2	43.2	43.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥16 Point Increase from Baseline in IBDQ Total Score at Week 8/ET Visit

End point title	Percentage of Participants with ≥16 Point Increase from Baseline in IBDQ Total Score at Week 8/ET Visit

End point description:

The IBDQ is a psychometrically validated PRO instrument for measuring disease-specific QOL in participants with IBD. IBDQ consists of 32 items, each item score ranged from 1 (worst possible response) to 7 (best possible response). Total score is the sum of each item score, and ranged from 32 to 224 with a higher score indicating a better QOL. Positive change in total score indicated improvement in QOL.

End point type	Secondary

End point timeframe:

Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	84	81	16
Units: Percentage of Participants				
number (not applicable)	61.4	75	76.5	75

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Response to the Patient-Reported Treatment Impact Assessment (PRTI) at Week 8/ET Visit by Category

End point title	Percentage of Participants with a Response to the Patient-Reported Treatment Impact Assessment (PRTI) at Week 8/ET Visit by Category

End point description:

The IBD Patient Reported Treatment Impact Modified (PRTI) questionnaire comprises 3 individual questions administered to the participant: participant satisfaction with study treatment; participant preference for study drug over prior treatment (this question on participant preference for study drug is prefaced by a simple question of previous treatment/s for IBD received in order to place the preference question into context) and participant willingness to re-use the study treatment again. Each of these questions (except the question on previous treatment, which is informational only) is scored on a 5 point

Likert scale. PSA = Patient Satisfaction Assessment; PPTA = Patient Previous Treatment Assessment; PPA = Patient Preference Assessment; PWA = Patient Willingness Assessment.

End point type	Secondary

End point timeframe:

Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	85	86	16
Units: Percentage of Participants				
number (not applicable)				
PSA: Extremely dissatisfied	17	6	7.4	6.3
PSA: Dissatisfied	10.2	9.6	6.2	0
PSA: Neither satisfied nor dissatisfied	25	19.3	16	25
PSA: Satisfied	40.9	45.8	43.2	25
PSA: Extremely satisfied	6.8	19.3	27.2	43.8
PPTA: Injectable prescription medicines	42	39.5	22.2	37.5
PPTA: Prescription medicines taken by mouth	37.5	44.4	56.8	43.8
PPTA: Surgery	2.3	2.5	0	0
PPTA: Prescription medicines and surgery	5.7	7.4	8.6	6.3
PPTA: No treatment	12.5	6.2	12.3	12.5
PPA: Definitely prefer the drug I receive now	33	42.2	48.1	56.3
PPA: Slight preference for drug I'm receiving now	19.3	27.7	22.2	25
PPA: I have no preference either way	28.4	19.3	13.6	18.8
PPA: Slight preference for previous treatment	9.1	2.4	7.4	0
PPA: No, definitely prefer my previous treatment	10.2	8.4	8.6	0
PWA: Would definitely want to use same drug again	44.3	53	61.7	50
PWA: Might want to use the same drug again	11.4	24.1	17.3	37.5
PWA: I am not sure	20.5	10.8	8.6	6.3
PWA: Might not want to use same drug again	6.8	2.4	4.9	0
PWA: Definitely not want to use same drug again	17	9.6	7.4	6.3

Statistical analyses

No statistical analyses for this end point

Secondary: Short Form 36 Health Survey (SF-36) Component and Domain Scores at Baseline and Week 8/ET Visit

End point title	Short Form 36 Health Survey (SF-36) Component and Domain Scores at Baseline and Week 8/ET Visit

End point description:

The component and domain scores were scored using the United States (US) 1998 general population norms. The resulting norm-based T scores for both the SF-36 version 2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	84	81	16
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Physical component score, Baseline	37.12 (± 7.66)	38.49 (± 6.78)	35.28 (± 8.49)	37.09 (± 9.14)
Physical component score, Week 8/ET	40.84 (± 9.23)	45.23 (± 8.85)	44.29 (± 9.41)	47.01 (± 7.97)
Mental Component Score, Baseline	36.5 (± 12.26)	34.85 (± 11.68)	35.84 (± 10.68)	39.26 (± 11.85)
Mental Component Score, Week 8/ET	42.46 (± 11.21)	43.69 (± 12.15)	43.65 (± 11.87)	42.73 (± 16.37)
Physical Functioning Domain, Baseline	43.73 (± 8.93)	43.56 (± 8.81)	41.36 (± 10.03)	42.66 (± 9.04)
Physical Functioning Domain, Week 8/ET	46.55 (± 8.93)	49.68 (± 8.43)	48.37 (± 8.78)	49.57 (± 8.99)
Role Physical Domain, Baseline	35.34 (± 9.94)	36.36 (± 9.71)	32.57 (± 10.92)	37.68 (± 12.43)
Role Physical Domain, Week 8/ET	39.92 (± 10.64)	44.49 (± 11.52)	42.84 (± 11.59)	44.39 (± 13.18)
Bodily Pain Domain, Baseline	34.69 (± 8.79)	35.22 (± 8.44)	33.32 (± 8.25)	34.98 (± 8.23)
Bodily Pain Domain, Week 8/ET	40.81 (± 10.43)	44.68 (± 11.29)	45.1 (± 10.41)	47.61 (± 11.21)
General Health Domain, Baseline	30.58 (± 7.21)	31.37 (± 7.15)	29.56 (± 7.52)	32.08 (± 12.42)
General Health Domain, Week 8/ET	34.36 (± 8.5)	36.79 (± 8.53)	37.19 (± 10.75)	37.98 (± 13.51)
Vitality Domain, Baseline	35.06 (± 9.7)	34.66 (± 7.86)	35.8 (± 9.05)	37.55 (± 11.88)
Vitality Domain, Week 8/ET	41.2 (± 11.45)	45.22 (± 11.94)	44.6 (± 12.53)	48.77 (± 13.41)
Social Functioning Domain, Baseline	34.71 (± 11.83)	35.53 (± 11.69)	33.83 (± 11.36)	35.9 (± 10.61)
Social Functioning Domain, Week 8/ET	40.02 (± 12.33)	45.01 (± 11.79)	43.46 (± 11.43)	43.63 (± 14.94)
Role Emotional Domain, Baseline	38.45 (± 13.98)	37.2 (± 12.96)	35.34 (± 13.23)	39.12 (± 14.02)
Role Emotional Domain, Week 8/ET	43.06 (± 12.43)	44.77 (± 12.46)	43.76 (± 11.94)	42.9 (± 16.58)
Mental Health Domain, Baseline	37.6 (± 12.3)	35.95 (± 11.38)	36.98 (± 11.09)	41.27 (± 10.27)
Mental Health Domain, Week 8/ET	43.75 (± 11.02)	43.58 (± 11.67)	44.76 (± 11.64)	43 (± 15.96)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline SF-36 Component and Domain Scores at Week 8/ET Visit Using ANCOVA

End point title	Change from Baseline SF-36 Component and Domain Scores at Week 8/ET Visit Using ANCOVA[9]

End point description:

The component and domain scores were scored using the US 1998 general population norms. The resulting norm-based T scores for both the SF-36 version 2 and SF-36 health domain scales and component summary measures have means of 50 and standard deviations of 10. Adjusted means were derived from the ANCOVA model with baseline value as a covariate, treatment group and prior use of anti-TNF alpha treatments as factors.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	84	81	
Units: Score on a Scale				
arithmetic mean (standard error)				
Physical component score	3.72 (± 0.927)	7.28 (± 0.967)	8.07 (± 0.956)	
Mental Component Score	6.47 (± 1.143)	7.88 (± 1.178)	7.13 (± 1.18)	
Physical Functioning Domain	3.01 (± 0.85)	6.14 (± 0.876)	5.59 (± 0.876)	
Role Physical Domain	5.02 (± 1.152)	8.76 (± 1.191)	8.95 (± 1.183)	
Bodily Pain Domain	6.41 (± 1.132)	9.94 (± 1.174)	11.1 (± 1.171)	
General Health Domain	3.62 (± 0.897)	5.55 (± 0.937)	7.03 (± 0.933)	
Vitality Domain	5.55 (± 1.19)	9.84 (± 1.225)	8.05 (± 1.233)	
Social Functioning Domain	5.25 (± 1.163)	9.72 (± 1.206)	8.66 (± 1.204)	
Role Emotional Domain	5.59 (± 1.222)	7.28 (± 1.257)	7.14 (± 1.26)	
Mental Health Domain	6.46 (± 1.1)	7.05 (± 1.136)	7.41 (± 1.134)	

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL 5 Dimensions Questionnaire (EQ-5D) Utility Scores at Baseline and Week 8/ET Visit

End point title	EuroQoL 5 Dimensions Questionnaire (EQ-5D) Utility Scores at Baseline and Week 8/ET Visit

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	85	86	16
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Utility Score, Baseline (n=89, 85, 86, 16)	0.56 (± 0.29)	0.58 (± 0.26)	0.49 (± 0.31)	0.61 (± 0.24)
Utility Score, Week 8/ET (n=85, 84, 80, 16)	0.64 (± 0.27)	0.71 (± 0.28)	0.71 (± 0.27)	0.77 (± 0.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline EQ-5D Utility Scores at Week 8/ET Visit Using ANCOVA

End point title	Change from Baseline EQ-5D Utility Scores at Week 8/ET Visit Using ANCOVA[10]

End point description:

EQ-5D: a participant rated questionnaire to assess health-related QoL via a single utility score. Health State Profile component assesses level of current health for 5 domains: mobility, self-care, usual activities, pain & discomfort, anxiety & depression; 1 = better health state (no problems); 3 = worst health state ("confined to bed"). Scoring formula developed by EuroQol Group assigns a utility value for each domain. Score is transformed to a total score ranging from -0.594 to 1.000; higher score indicates better health state. Adjusted means were derived from the ANCOVA model with baseline value as a covariate, treatment group & prior use of anti-TNFα treatments as factors.The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	84	80	
Units: Score on a Scale				
arithmetic mean (standard error)	0.08 (± 0.029)	0.14 (± 0.03)	0.16 (± 0.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Visual Analogue Scale (VAS) Scores at Baseline and Week 8/ET Visit

End point title	EQ-5D Visual Analogue Scale (VAS) Scores at Baseline and Week 8/ET Visit

End point description:

EQ-5D is a participant rated questionnaire to assess health-related QoL in terms of a single index value. The VAS component rates current health state on a scale from 0 millimeters (mm) (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a better health state. Number of Subjects Analysed is the maximum number of participants with non-missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Tofacitinib 15 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	85	86	16
Units: mm				
arithmetic mean (standard deviation)				
VAS Score, Baseline (n=90, 85, 86, 16)	46.83 (± 18.63)	49.51 (± 18.03)	42.74 (± 18.04)	52.06 (± 24.11)
VAS Score, Week 8/ET (n=85, 83, 81, 16)	58.32 (± 21.31)	67.07 (± 19.39)	65.77 (± 19.71)	69.81 (± 21.11)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline EQ-5D VAS Scores at Week 8/ET Visit Using ANCOVA

End point title	Change from Baseline EQ-5D VAS Scores at Week 8/ET Visit Using ANCOVA[11]

End point description:

EQ-5D is a participant rated questionnaire to assess health-related QoL in terms of a single index value. The VAS component rates current health state on a scale from 0 millimeters (mm) (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a better health state. Adjusted means were derived from the ANCOVA model with baseline value as a covariate, treatment

group & prior use of anti-TNF alpha treatments as factors.
The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point type	Secondary

End point timeframe:

Baseline, Week 8/ET visit

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 15 mg BID treatment group was closed to further enrolment early on in the study by Protocol Amendment 5 after only 16 participants were enrolled into this group. Therefore, the efficacy analysis was not performed for this group because the results may be difficult to interpret due to the small sample size.

End point values	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	83	81	
Units: mm				
arithmetic mean (standard error)	11.97 (± 2.166)	19.56 (± 2.252)	20.62 (± 2.222)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were assessed from informed consent through and including 28 calendar days after last administration of study treatment (i.e. 11 weeks). Non-SAEs were recorded from time of first dose of study treatment through last participant visit (i.e. 15 weeks).

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo tablets to match tofacitinib 5 mg for oral administration BID for 8 weeks.

Reporting group title	Tofacitinib 5 mg BID

Reporting group description:

Tofacitinib tablets for oral administration at a dose of 5 mg BID for 8 weeks.

Reporting group title	Tofacitinib 10 mg BID

Reporting group description:

Tofacitinib tablets for oral administration at a dose of 10 mg BID for 8 weeks.

Reporting group title	Tofacitinib 15 mg BID

Reporting group description:

Tofacitinib tablets for oral administration at a dose of 15 mg BID for 8 weeks.

Serious adverse events	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 91 (3.30%)	3 / 86 (3.49%)	10 / 86 (11.63%)
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)			
Breast cancer			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fistula			

subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn’s disease			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (0.00%)	3 / 86 (3.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urethral			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
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			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	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
Anal abscess			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (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
Gastroenteritis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	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
Perirectal abscess			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (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
Pneumonia influenzal			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Tofacitinib 15 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn’s disease			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urethral			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Perirectal abscess			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia influenzal			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 91 (47.25%)	37 / 86 (43.02%)	42 / 86 (48.84%)
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 91 (2.20%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	2	0	0
Hypertension			
subjects affected / exposed	1 / 91 (1.10%)	4 / 86 (4.65%)	1 / 86 (1.16%)
occurrences (all)	1	4	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 91 (2.20%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	3	2	2
Chills			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 91 (1.10%)	3 / 86 (3.49%)	3 / 86 (3.49%)
occurrences (all)	1	3	3
Pyrexia			
subjects affected / exposed	3 / 91 (3.30%)	2 / 86 (2.33%)	5 / 86 (5.81%)
occurrences (all)	3	2	5
Tenderness			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed[1]	1 / 60 (1.67%)	0 / 86 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 91 (2.20%)	2 / 86 (2.33%)	2 / 86 (2.33%)
occurrences (all)	2	2	2
Rhinorrhoea			

subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Blood triglycerides increased			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 91 (0.00%)	2 / 86 (2.33%)	0 / 86 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 91 (3.30%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	3	1	3
Headache			
subjects affected / exposed	7 / 91 (7.69%)	8 / 86 (9.30%)	5 / 86 (5.81%)
occurrences (all)	9	8	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 91 (1.10%)	4 / 86 (4.65%)	2 / 86 (2.33%)
occurrences (all)	1	4	2
Lymphadenopathy			

subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	5 / 91 (5.49%)	3 / 86 (3.49%)	7 / 86 (8.14%)
occurrences (all)	5	5	9
Abdominal tenderness			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (0.00%)	2 / 86 (2.33%)
occurrences (all)	1	0	2
Anal fistula			
subjects affected / exposed	0 / 91 (0.00%)	2 / 86 (2.33%)	1 / 86 (1.16%)
occurrences (all)	0	2	1
Aphthous stomatitis			
subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 91 (1.10%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences (all)	1	1	1
Crohn’s disease			
subjects affected / exposed	6 / 91 (6.59%)	5 / 86 (5.81%)	4 / 86 (4.65%)
occurrences (all)	6	7	4
Diarrhoea			
subjects affected / exposed	3 / 91 (3.30%)	1 / 86 (1.16%)	0 / 86 (0.00%)
occurrences (all)	3	1	0
Dyspepsia			
subjects affected / exposed	1 / 91 (1.10%)	2 / 86 (2.33%)	2 / 86 (2.33%)
occurrences (all)	1	2	2
Flatulence			

subjects affected / exposed	1 / 91 (1.10%)	2 / 86 (2.33%)	2 / 86 (2.33%)
occurrences (all)	1	2	2
Nausea			
subjects affected / exposed	8 / 91 (8.79%)	5 / 86 (5.81%)	7 / 86 (8.14%)
occurrences (all)	8	5	7
Stomatitis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 91 (1.10%)	4 / 86 (4.65%)	5 / 86 (5.81%)
occurrences (all)	1	4	5
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	2 / 91 (2.20%)	2 / 86 (2.33%)	0 / 86 (0.00%)
occurrences (all)	2	2	0
Rash maculo-papular			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 91 (2.20%)	2 / 86 (2.33%)	2 / 86 (2.33%)
occurrences (all)	3	2	2
Back pain			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Joint swelling			

subjects affected / exposed	1 / 91 (1.10%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 91 (0.00%)	2 / 86 (2.33%)	0 / 86 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	2 / 91 (2.20%)	1 / 86 (1.16%)	0 / 86 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 86 (1.16%)	3 / 86 (3.49%)
occurrences (all)	0	1	3
Folliculitis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 86 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	2 / 91 (2.20%)	1 / 86 (1.16%)	1 / 86 (1.16%)
occurrences (all)	2	1	1
Nasopharyngitis			
subjects affected / exposed	3 / 91 (3.30%)	3 / 86 (3.49%)	6 / 86 (6.98%)
occurrences (all)	3	4	6
Oral candidiasis			
subjects affected / exposed	1 / 91 (1.10%)	2 / 86 (2.33%)	1 / 86 (1.16%)
occurrences (all)	1	2	1
Oral herpes			
subjects affected / exposed	2 / 91 (2.20%)	0 / 86 (0.00%)	0 / 86 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	5 / 91 (5.49%)	1 / 86 (1.16%)	2 / 86 (2.33%)
occurrences (all)	6	1	2

Non-serious adverse events	Tofacitinib 15 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)		
Vascular disorders			

Flushing subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Hypertension subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Fatigue subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Tenderness subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Reproductive system and breast disorders Ovarian cyst subjects affected / exposed[1] occurrences (all)	0 / 16 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) Blood triglycerides increased subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0 1 / 16 (6.25%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0 1 / 16 (6.25%) 1		
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Abdominal tenderness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Anal fistula			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Aphthous stomatitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Crohn’s disease			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nausea			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Muscle spasms			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	5		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only female participants were counted as exposed to this adverse event of ovarian cyst.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2011	Amendment 1 was country-specific to Japan and added specific safety screening and monitoring requirements.
07 September 2011	Amendment 2 corrected an error in the first question of the CDAI (the primary endpoint assessment tool) to add the word "very," which had been inadvertently omitted, before the words "soft stools." Language regarding publication policy was also added to meet requirements for all countries involved in this study. The opportunity was then taken to also correct other minor typographical errors and clarify some language that was felt to be imprecise or unclear in the protocol.
02 July 2012	Amendment 3 was a country-specific amendment for India and the Netherlands that excluded subjects over 65 years of age.
28 September 2012	Amendment 4 updated standard Pfizer protocol text, including safety language in various sections. An updated prohibited medication table was also included, as were lymphocyte count requirements for subject selection and monitoring, discontinuation criteria for lymphopenia, guidance regarding surgery during the study, and updates to the background section.
16 November 2012	Amendment 5 removed the tofacitinib 15 mg BID dose group and updated the statistical methods and dose rationale sections accordingly. This amendment also revised the country-specific upper age limit for India.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported