



Clinical trial results:

A Open-Label Extension Study of CP-690,550 as Maintenance Therapy in Patients with Crohn's Disease

Summary

EudraCT number	2011-003622-27
Trial protocol	SE ES HU DE CZ BG GR NL AT HR
Global end of trial date	25 July 2016

Results information

Result version number	v1 (current)
This version publication date	09 July 2017
First version publication date	09 July 2017

Trial information

Trial identification

Sponsor protocol code	A3921086
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01470599
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 July 2016
Global end of trial reached?	Yes
Global end of trial date	25 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the safety and tolerability of long-term open label tofacitinib therapy in subjects with Crohn's disease. Secondary objectives were to evaluate the effect of open-label (OL) tofacitinib maintenance therapy on clinical remission in subjects with Crohn's disease, to evaluate the effect of OL tofacitinib maintenance therapy on quality of life in subjects with Crohn's disease and to evaluate the effect of OL tofacitinib maintenance therapy on biomarkers as measured by C-reactive protein (CRP) and fecal calprotectin.

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 Harmonisation Good Clinical Practice 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) and/or Independent Ethics Committee(s) at each of the investigational centres participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 April 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	Australia: 5
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Spain: 14

Country: Number of subjects enrolled	Ukraine: 5
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	150
EEA total number of subjects	56

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)	148
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in participants who completed the 26-week maintenance treatment of Study A3921084 or who withdrew early due to A3921084 study treatment failure according to prespecified criteria.

Pre-assignment

Screening details:

Participants were assigned to either the 5 milligrams (mg) twice daily (BID) or 10 mg BID treatment group according to clinical remission status as assessed by Crohn's Disease Activity Index (CDAI) score at the end of the A3921084 study treatment visit or early termination visit due to A3921084 study treatment failure.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

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

Arm description:

Tofacitinib 5 mg tablet for oral administration at a dose of 5 mg BID for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	CP-690550-10
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At the baseline visit, eligible subjects were assigned to the appropriate dose based on CDAI score assessed at the final visit in study A3921084. Subjects with a CDAI total score less than (<) 150 were allocated to the tofacitinib 5 mg BID dose for up to 48 weeks. There was a single dose adjustment allowed (at the discretion of the investigator) from 5 mg BID to 10 mg BID, after the initial 8 weeks of fixed OL treatment and for the remaining treatment period of 40 weeks.

Arm title	Tofacitinib 10 mg BID
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Arm description:

Tofacitinib 10 mg tablets (2 x 5 mg tablets) for oral administration at a dose of 10 mg BID for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Tofacitinib
Investigational medicinal product code	CP-690550-10
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

At the baseline visit, eligible subjects were assigned to the appropriate dose based on CDAI score assessed at the final visit in study A3921084. Subjects with a CDAI total score greater than or equal to (\geq) 150 were allocated to the tofacitinib 10 mg BID dose for up to 48 weeks. There was a single dose adjustment allowed (at the discretion of the investigator) from 10 mg BID to 5 mg BID, after the initial 8 weeks of fixed OL treatment and for the remaining treatment period of 40 weeks.

Number of subjects in period 1	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
Started	62	88
Completed	43	45
Not completed	19	43
Consent withdrawn by subject	3	4
Did not meet entrance criteria	1	-
Adverse event not related to study drug	1	5
Unspecified	1	-
Lost to follow-up	2	1
Adverse event related to study drug	2	5
Protocol deviation	3	1
Insufficient clinical response	6	27

Baseline characteristics

Reporting groups

Reporting group title	Tofacitinib 5 mg BID
Reporting group description: Tofacitinib 5 mg tablet for oral administration at a dose of 5 mg BID for up to 48 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description: Tofacitinib 10 mg tablets (2 x 5 mg tablets) for oral administration at a dose of 10 mg BID for up to 48 weeks.	

Reporting group values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Total
Number of subjects	62	88	150
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)	61	87	148
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	41	38.2	
standard deviation	± 12.6	± 11.6	-
Gender, Male/Female			
Units: Subjects			
Female	30	41	71
Male	32	47	79

End points

End points reporting groups

Reporting group title	Tofacitinib 5 mg BID
Reporting group description: Tofacitinib 5 mg tablet for oral administration at a dose of 5 mg BID for up to 48 weeks.	
Reporting group title	Tofacitinib 10 mg BID
Reporting group description: Tofacitinib 10 mg tablets (2 x 5 mg tablets) for oral administration at a dose of 10 mg BID for up to 48 weeks.	

Primary: Adjudicated Potential Cardiovascular Events

End point title	Adjudicated Potential Cardiovascular Events ^[1]
End point description: Pre-specified cardiovascular events were adjudicated by committees of external experts who were blinded to treatment assignment. Potential events of interest (pEoI) were identified by the investigator, sponsor, review of alerts from central electrocardiogram assessments, and by search of adverse events (AE)/serious adverse event (SAE) listings for events coded to death (coronary and non-coronary), myocardial infarction (non-fatal), all coronary revascularization, unstable angina, stroke (fatal and non-fatal), transient ischemic attack, congestive heart failure, peripheral arterial vascular disease, dyspnoea, and chest pain. The independent reviewers (IRs) determined if the pEoI met the criteria for EoI classification according to the definitions summarized from the Clinical Data Interchange Standards Consortium 'Standardized Definitions for End Point Events in Cardiovascular Trials' published October 2010.	
End point type	Primary
End point timeframe: From baseline to Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	2		
Units: Number of participants meeting criteria		0		

Notes:

[2] - No cardiovascular events were adjudicated.

Statistical analyses

No statistical analyses for this end point

Primary: Adjudicated Malignancy Events

End point title	Adjudicated Malignancy Events ^[3]
End point description: Pre-specified malignancy events were adjudicated by committees of external experts who were blinded to treatment assignment. pEoI were identified by the investigator, sponsor, potential primary event notifications (i.e. malignancies excluding non-melanoma skin cancers) for a specific protocol, events submitted for histopathology review for potential malignancies which met the criteria for potential malignancies, and by search of AE/SAE listings for events coded to Malignant tumors Standard Medical	

Dictionary for Regulatory Activities (MedDRA) Queries (SMQ) (20000194). IRs determined if the pEoI met the criteria for EoI classification according to the International Classification of Diseases for Oncology, a ten-digit multi-axial classification of the site (4 characters), morphology (4 digits), behavior (1 digit), and grading (1 digit) of neoplasms.

End point type	Primary
End point timeframe:	
From baseline to Week 52	

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: Number of participants meeting criteria	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Adjudicated Hepatic Injury Events

End point title	Adjudicated Hepatic Injury Events ^[4]
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End point description:

Pre-specified liver injury events were adjudicated by blinded committees of external experts. pEoI(s) were identified by investigator, sponsor & search of clinical, safety & laboratory databases (potential Hy's law event, ALT/AST $\geq 5 \times$ ULN, events meeting hepatic discontinuation criteria, SAEs coded to MedDRA hepatobiliary system organ class (SOC), AEs/SAEs coded to MedDRA liver infections or infectious biliary disorders SMQ, AEs coded to MedDRA drug-induced liver injury (DILI) preferred term or any death with ALT or AST $\geq 3 \times$ ULN, bilirubin $\geq 2 \times$ ULN or jaundice). IRs determined if the pEoI met the criteria for EoI classification by assessing DILI (definite, highly likely, probable, possible, unlikely, unrelated or undetermined), pattern (hepatocellular, mixed, cholestatic or undetermined), likely, competing or alternative cause(s), severity (mild, moderate, severe, fatal/transplantation or undetermined), Hy's law case, recovery & liver failure (all yes, no or undetermined).

End point type	Primary
End point timeframe:	
From baseline to Week 52	

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[5]	1		
Units: Number of participants meeting criteria		0		

Notes:

[5] - No hepatic injury events were adjudicated.

Statistical analyses

No statistical analyses for this end point

Primary: Adjudicated Opportunistic Infection Events

End point title	Adjudicated Opportunistic Infection Events ^[6]
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End point description:

Pre-specified opportunistic infection events were adjudicated by blinded committees of external experts. pEoI(s) were identified by investigator, sponsor & search of SAE listings for serious infections coded to MedDRA infections & infestations SOC &/or events meeting pre-specified criteria for IR pre-screening to determine if adjudication is required. IRs determined if the pEoI met the criteria for EoI classification according to definitions for opportunistic infections (invasive fungal infections per the European Organization for Research & Treatment of Cancer/Invasive Fungal Infections Cooperative Group & the National Institute of Allergy & Infectious Diseases Mycoses Study Group [EORTC/MSG] Consensus Group definitions, endemic fungal infections per the EORTC/MSG Consensus Group definitions, other fungal infections, viral, bacterial & parasitic infections & vaccine dissemination) & special interest infections (actinomycosis, Legionella & mononucleosis-like toxoplasmosis).

End point type	Primary
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End point timeframe:

From baseline to Week 52

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: Number of participants meeting criteria	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Adjudicated Gastrointestinal (GI) Perforation Events

End point title	Adjudicated Gastrointestinal (GI) Perforation Events ^[7]
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End point description:

Pre-specified GI perforation events were adjudicated by committees of external experts who were blinded to treatment assignment. The pEoI(s) were identified for IR via search of AE/SAE listings using the MedDRA GI Perforation SMQ. The IRs determined if the pEoI met the criteria for EoI classification based on whether a GI perforation occurred and if yes, the location within the GI tract, possible contributing medical conditions and/or concomitant medications.

End point type	Primary
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End point timeframe:

From baseline to Week 52

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	2		
Units: Number of participants meeting criteria		2		

Notes:

[8] - No GI perforation events were adjudicated.

Statistical analyses

No statistical analyses for this end point

Primary: Adjudicated Interstitial Lung Disease (ILD) Events

End point title	Adjudicated Interstitial Lung Disease (ILD) Events ^[9]
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End point description:

Pre-specified ILD events were adjudicated by committees of external experts who were blinded to treatment assignment. pEoI were identified by searches of the clinical, safety & laboratory databases (AEs coded to the MedDRA ILD SMQ and events nominated by the study clinician or clinical lead). The IRs determined if the pEoI met the criteria for EoI classification by assessment of the ILD event (probably ILD, possible ILD, alternative diagnosis likely, other or insufficient information to classify).

End point type	Primary
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End point timeframe:

From baseline to Week 52

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per the protocol, the planned analysis was descriptive only.

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: Number of participants meeting criteria				

Notes:

[10] - No ILD events were adjudicated.

[11] - No ILD events were adjudicated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission and Sustained Clinical Remission at Week 48

End point title	Percentage of Participants in Clinical Remission and Sustained Clinical Remission at Week 48
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End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. Clinical remission was defined as a CDAI score of < 150. Sustained clinical remission was defined as being in clinical remission (CDAI score <150) at both Week 24 and Week 48. 95 percent (%) Clopper-Pearson exact confidence interval reported for the proportions. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Week 48

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Percent				
number (confidence interval 95%)				
Clinical remission (n=33, 36)	87.88 (71.8 to 96.6)	55.56 (38.1 to 72.06)		
Sustained clinical remission (n=32, 35)	75 (56.6 to 88.54)	34.29 (19.13 to 52.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission and Sustained Clinical Remission Among Participants in Clinical Remission at Baseline of this Study

End point title	Percentage of Participants in Clinical Remission and Sustained Clinical Remission Among Participants in Clinical Remission at Baseline of this Study
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End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. Clinical remission was defined as a CDAI score of <150. Sustained clinical remission was defined as being in clinical remission (CDAI score <150) at both Week 24 and Week 48. 95% Clopper-Pearson exact confidence interval reported for the proportions. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	4		
Units: Percentage of participants				
number (confidence interval 95%)				
Clinical remission: Baseline (n=61, 4)	100 (94.13 to 100)	100 (39.76 to 100)		
Clinical remission: Week 8 (n=53, 4)	75.47 (61.72 to 86.24)	50 (6.76 to 93.24)		
Clinical remission: Week 16 (n=52, 4)	84.62 (71.92 to 93.12)	75 (19.41 to 99.37)		
Clinical remission: Week 24 (n=48, 4)	85.42 (72.24 to 93.93)	25 (0.63 to 80.59)		

Clinical remission: Week 36 (n=40, 3)	92.5 (79.61 to 98.43)	33.33 (0.84 to 90.57)		
Clinical remission: Week 48 (n=32, 3)	87.5 (71.01 to 96.49)	100 (29.24 to 100)		
Clinical remission: Week 52/follow-up (n=37, 3)	64.86 (47.46 to 79.79)	33.33 (0.84 to 90.57)		
Sustained clinical remission (n=31, 3)	77.42 (58.9 to 90.41)	33.33 (0.84 to 90.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in Clinical Remission and Sustained Clinical Remission Among Participants in Clinical Response (CDAI-100 Response) or Clinical Remission at Baseline of this Study

End point title	Percentage of Participants in Clinical Remission and Sustained Clinical Remission Among Participants in Clinical Response (CDAI-100 Response) or Clinical Remission at Baseline of this Study
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End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. Clinical remission was defined as a CDAI score of <150. Sustained clinical remission was defined as being in clinical remission (CDAI score <150) at both Week 24 and Week 48. Clinical response was defined as a CDAI score reduction of at least 100 points from the A3921083 study baseline value. 95% Clopper-Pearson exact confidence interval reported for the proportions. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	23		
Units: Percent				
number (confidence interval 95%)				
Clinical remission: Baseline (n=62, 23)	98.39 (91.34 to 99.96)	17.39 (4.95 to 38.78)		
Clinical remission: Week 8 (n=54, 20)	75.93 (62.36 to 86.51)	35 (15.39 to 59.22)		
Clinical remission: Week 16 (n=53, 19)	84.91 (72.41 to 93.25)	36.84 (16.29 to 61.64)		
Clinical remission: Week 24 (n=49, 16)	83.67 (70.34 to 92.68)	43.75 (19.75 to 70.12)		
Clinical remission: Week 36 (n=41, 13)	90.24 (76.87 to 97.28)	38.46 (13.86 to 68.42)		
Clinical remission: Week 48 (n=33, 10)	87.88 (71.8 to 96.6)	50 (18.71 to 81.29)		
Clinical remission: Week 52/follow-up (n=38, 12)	65.79 (48.65 to 80.37)	41.67 (15.17 to 72.33)		

Sustained clinical remission (n=32, 10)	75 (56.6 to 88.54)	30 (6.67 to 62.25)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Time to Relapse Among Participants in Clinical Remission at Baseline

End point title	Time to Relapse Among Participants in Clinical Remission at Baseline
End point description:	
Relapse was defined as an increase in CDAI of more than (>) 100 points from the baseline and an absolute CDAI score of >220 points. CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. Data presented are rates estimated from Kaplan-Meier curves. n = number of participants remaining at risk. 9999 = not applicable, no participants had a relapse event by Week 8. 99999 = not applicable, no participants remained at risk of a relapse event at Week 48.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	4		
Units: Percent				
number (confidence interval 95%)				
Week 8 (n=55, 4)	6.78 (3.38 to 11.78)	9999 (9999 to 9999)		
Week 16 (n=51, 3)	11.86 (7.15 to 17.87)	25 (4.56 to 53.66)		
Week 24 (n=46, 3)	15.46 (9.98 to 22.05)	25 (4.56 to 53.66)		
Week 36 (n=38, 3)	21.42 (14.82 to 28.83)	25 (4.56 to 53.66)		
Week 48 (n=7, 0)	24.69 (17.21 to 32.89)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed CDAI Score by Week

End point title	Observed CDAI Score by Week
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End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. n = number of participants remaining at risk.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=62, 88)	77.13 (± 43.22)	291.19 (± 95.78)		
Week 8 (n=54, 75)	105.39 (± 75.82)	176.96 (± 82.39)		
Week 16 (n=53, 66)	86.58 (± 65.23)	178.94 (± 72.25)		
Week 24 (n=49, 59)	85.12 (± 56.67)	163.66 (± 79.73)		
Week 36 (n=41, 48)	73.34 (± 59.52)	158.67 (± 89.15)		
Week 48 (n=33, 36)	73.91 (± 70.23)	154.11 (± 71.47)		
Week 52/Follow-up (n=38, 43)	129.32 (± 114.82)	180.65 (± 98.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Observed CDAI Score by Week

End point title	Change from Baseline Observed CDAI Score by Week
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End point description:

CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 8 (n=54, 75)	26.96 (± 62.68)	-114.31 (± 112.44)		
Week 16 (n=53, 66)	11.72 (± 52.25)	-112.02 (± 111.09)		
Week 24 (n=49, 59)	6.33 (± 44.48)	-122.69 (± 117.65)		
Week 36 (n=41, 48)	-10.78 (± 40.35)	-139.81 (± 126.18)		
Week 48 (n=33, 36)	-4.79 (± 60.09)	-121.94 (± 129.21)		
Week 52/Follow-up (n=38, 43)	47.66 (± 109.73)	-107.42 (± 119.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Steroid-Free Clinical Remission at Week 48 - Among Subjects on Steroids at A3921086 Baseline

End point title	Percentage of Participants Achieving a Steroid-Free Clinical Remission at Week 48 - Among Subjects on Steroids at A3921086 Baseline
End point description:	Steroid-free clinical remission at Week 48 was a CDAI <150 points in participants who were steroid-free at Week 48. CDAI is a composite index consisting of weighted scoring of 8 disease variables: number of liquid or very soft stools, intensity of abdominal pain, general well-being, occurrence of extraintestinal 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:	
Week 48	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	11		
Units: Percent				
number (confidence interval 95%)	50 (1.26 to 98.74)	9.09 (0.23 to 41.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Corticosteroid Use over Time

End point title	Corticosteroid Use over Time
End point description: Use of corticosteroids (yes or no) as recorded at baseline and throughout the study.	
End point type	Secondary
End point timeframe: Weeks 8, 16, 24, 36 and 48	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Percentage of participants				
number (not applicable)				
Baseline	1.61	20.45		
Week 8	4.84	21.59		
Week 16	4.84	13.64		
Week 24	4.84	12.5		
Week 36	3.23	10.23		
Week 48	1.61	7.95		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Switching from 5 mg BID to 10 mg BID or 10 mg BID to 5 mg BID after Initial Assignment by Visit

End point title	Percentage of Participants Switching from 5 mg BID to 10 mg BID or 10 mg BID to 5 mg BID after Initial Assignment by Visit
End point description: There was a single study treatment dose adjustment allowed, at the discretion of the Investigator, from 5 mg BID to 10 mg BID or from 10 mg BID to 5 mg BID, after the initial 8 weeks of fixed open label treatment and for the remaining treatment period of 40 weeks.	
End point type	Secondary
End point timeframe: From baseline to Week 48	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Percentage of participants				
number (not applicable)				
Baseline	0	0		
Week 8	25.81	0		
Week 16	6.45	0		
Week 24	3.23	2.27		
Week 36	0	1.14		
Week 48	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Change From Baseline in Fecal Calprotectin by Week

End point title	Observed Change From Baseline in Fecal Calprotectin by Week
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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. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: mg per kilogram (mg/kg)				
arithmetic mean (standard deviation)				
Week 8 (n=53, 71)	-105.51 (± 436.41)	-102.82 (± 310.1)		
Week 16 (n=54, 64)	-144.65 (± 423.2)	-35.28 (± 718.82)		
Week 24 (n=49, 55)	-120.49 (± 511.49)	-130.68 (± 337.23)		
Week 36 (n=41, 42)	-169.92 (± 354.3)	-133.82 (± 364.51)		
Week 48 (n=37, 38)	-189.61 (± 462.61)	-123.87 (± 376.7)		
Week 52/Follow-up (n=48, 57)	-51.33 (± 453.73)	-109.23 (± 389.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Change From Baseline in High Sensitivity CRP by Week

End point title	Observed Change From Baseline in High Sensitivity CRP by Week
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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. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 8, 16, 24, 36, 48 and 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: mg per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 8 (n=61, 82)	-0.44 (± 14.78)	-4.81 (± 26.76)		
Week 16 (n=58, 72)	-2.46 (± 14.54)	-7.96 (± 25.11)		
Week 24 (n=54, 61)	-2.76 (± 17.59)	-9.26 (± 30.2)		
Week 36 (n=46, 51)	-4.42 (± 22.29)	-12.09 (± 30.61)		
Week 48 (n=43, 44)	-4.55 (± 17.81)	-11.45 (± 31.3)		
Week 52/Follow-up (n=54, 71)	3.86 (± 21.57)	-4.72 (± 31.34)		

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 48/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 48/ET Visit
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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). The 32 items are grouped into 4 domains: bowel function, emotional status, systemic symptoms and social function. The 4 domains are scored as follows: bowel symptoms 10 to 70; systemic symptoms 5 to 35; emotional function 12 to 84; social function 5 to 35. For each domain, a higher score indicates better QoL. 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.
n = number of participants with non-missing data.

End point type	Secondary
End point timeframe:	
Baseline and Week 48/early termination (ET)	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
IBDQ Total Score, Baseline (n=62, 87)	187.23 (± 20.38)	127.32 (± 34.17)		
IBDQ Total Score, Week 48/ET (n=57, 83)	179.26 (± 29.89)	144.42 (± 42.16)		
Bowel Function Score, Baseline (n=62, 87)	58.56 (± 6.86)	40.71 (± 9.9)		
Bowel Function Score, Week 48/ET (n=57, 83)	55.7 (± 9.82)	46.7 (± 12.38)		
Emotional Status Score, Baseline (n=62, 87)	69.68 (± 8.58)	48.61 (± 14.42)		
Emotional Status Score, Week 48/ET (n=57, 83)	66.98 (± 12.27)	53.19 (± 17.32)		
Systemic Symptoms Score, Baseline (n=62, 87)	26.95 (± 5.36)	17.2 (± 5.55)		
Systemic Symptoms Score, Week 48/ET (n=57, 83)	25.82 (± 6.28)	20.35 (± 7.07)		
Social Function Score, Baseline (n=62, 87)	32.03 (± 3.59)	20.8 (± 8.96)		
Social Function Score, Week 48/ET (n=57, 83)	30.75 (± 5.17)	24.18 (± 8.98)		

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 48/ET Visit

End point title	Change from Baseline IBDQ Total Score and Domain Scores (Bowel Function, Emotional Status, Systemic Symptoms, and Social Function) at Week 48/ET Visit
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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). The 32 items are grouped into 4 domains: bowel function, emotional status, systemic symptoms and social function. The 4 domains are scored as follows: bowel symptoms 10 to 70; systemic symptoms 5 to 35; emotional function 12 to 84; social function 5 to 35. For each domain, a higher score indicates better QoL. 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
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End point timeframe:
Baseline and Week 48/ET

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	83		
Units: Score on a scale				
arithmetic mean (standard deviation)				
IBDQ Total Score, Week 48/ET	-7.98 (± 24.93)	18.84 (± 40.45)		
Bowel Function Score, Week 48/ET	-2.72 (± 8.3)	6.37 (± 12.41)		
Emotional Status Score, Week 48/ET	-3.07 (± 10.48)	5.36 (± 15)		
Systemic Symptoms Score, Week 48/ET	-1 (± 4.83)	3.45 (± 7.43)		
Social Function Score, Week 48/ET	-1.19 (± 4.24)	3.66 (± 8.89)		

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 48/ET Visit

End point title	Percentage of Participants with an IBDQ Total Score of Greater than or Equal to (≥) 170 at Week 48/ET Visit
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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. A score ≥170 corresponds to clinical remission. 95% Clopper-Pearson exact confidence interval reported for the proportions.

End point type	Secondary
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End point timeframe:

Week 48/ET

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	83		
Units: Percentage of participants				
number (confidence interval 95%)	70.18 (56.6 to 81.57)	31.33 (21.59 to 42.44)		

Statistical analyses

Secondary: Percentage of Participants with a Response to the Patient-Reported Treatment Impact (PRTI) Assessment at Week 48/ET Visit by Category

End point title	Percentage of Participants with a Response to the Patient-Reported Treatment Impact (PRTI) Assessment at Week 48/ET Visit by Category
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End point description:

The IBD PRTI modified 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 reuse 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
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End point timeframe:

Week 48/ET visit

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	46		
Units: Percentage of participants				
number (not applicable)				
PSA: Extremely dissatisfied	0	0		
PSA: Dissatisfied	0	8.7		
PSA: Neither satisfied nor dissatisfied	0	17.4		
PSA: Satisfied	33.3	41.3		
PSA: Extremely satisfied	66.7	32.6		
PPTA: Injectable prescription medicines	40.5	32.6		
PPTA: Prescription medicines taken by mouth	45.2	43.5		
PPTA: Surgery	2.4	0		
PPTA: Prescription medicines & surgery	7.1	13		
PPTA: No treatment	4.8	10.9		
PPA: Definitely prefer the drug I am receiving now	88.1	56.5		
PPA: Slight preference for drug I'm receiving now	4.8	21.7		
PPA: I have no preference either way	7.1	17.4		
PPA: Slight preference for previous treatment	0	4.3		
PPA: No, I definitely prefer my previous treatment	0	0		
PWA: Would definitely want to use same drug again	83.3	60.9		
PWA: Might want to use the same drug again	14.3	23.9		
PWA: I am not sure	2.4	10.9		
PWA: Might not want to use same drug again	0	0		

PWA: Definitely not want to use same drug again	0	4.3		
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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 48/ET Visit

End point title	Short Form 36 Health Survey (SF-36) Component and Domain Scores at Baseline and Week 48/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 SF36 version 2 and SF36 health domain scales and component summary measures have means of 50 and standard deviations of 10. Higher scores indicate better health-related QoL. n = number of participants with non-missing data.	
End point type	Secondary
End point timeframe: Baseline and Week 48/ET visit	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Physical component score, Baseline (n=62, 86)	50.15 (± 6.73)	37.8 (± 9.53)		
Physical component score, Week 48/ET (n=57, 83)	48.43 (± 8.22)	41.87 (± 10.06)		
Mental Component Score, Baseline (n=62, 86)	50.25 (± 9.11)	37.17 (± 11.94)		
Mental Component Score, Week 48/ET (n=57, 83)	48.79 (± 10.64)	39.6 (± 12.87)		
Physical Functioning Domain, Baseline (n=62, 86)	53.35 (± 5.5)	43.5 (± 10.37)		
Physical Functioning Domain, Week 48/ET (n=57, 83)	51.4 (± 8.59)	46.81 (± 10.22)		
Role Physical Domain, Baseline (n=62, 86)	50.97 (± 8.22)	35.93 (± 11.3)		
Role Physical Domain, Week 48/ET (n=57, 83)	49.38 (± 8.78)	40.04 (± 12.99)		
Bodily Pain Domain, Baseline (n=62, 87)	51.32 (± 8.55)	35.31 (± 9.14)		
Bodily Pain Domain, Week 48/ET (n=57, 83)	49.57 (± 10.3)	41.04 (± 12.69)		
General Health Domain, Baseline (n=62, 87)	41.6 (± 9.51)	31.74 (± 8.41)		
General Health Domain, Week 48/ET (n=57, 83)	40.39 (± 10.08)	33.45 (± 10.16)		

Vitality Domain, Baseline (n=62, 87)	52.78 (± 10.68)	36.92 (± 9.88)		
Vitality Domain, Week 48/ET (n=57, 83)	51.06 (± 11.38)	41.03 (± 12.38)		
Social Functioning Domain, Baseline (n=62, 87)	51.81 (± 7.21)	36.38 (± 12.29)		
Social Functioning Domain, Week 48/ET (n=57, 83)	49.42 (± 9.64)	39.82 (± 13.39)		
Role Emotional Domain, Baseline (n=62, 86)	50.12 (± 8.85)	38.55 (± 12.73)		
Role Emotional Domain, Week 48/ET (n=57, 83)	47.97 (± 10.78)	41.13 (± 13.15)		
Mental Health Domain, Baseline (n=62, 87)	49.89 (± 9.84)	37.61 (± 11.98)		
Mental Health Domain, Week 48/ET (n=57, 83)	49.24 (± 10.27)	40.13 (± 12.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline SF-36 Component and Domain Scores at Week 48/ET Visit

End point title	Change from Baseline SF-36 Component and Domain Scores at Week 48/ET Visit
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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 SF36 version 2 and SF36 health domain scales and component summary measures have means of 50 and standard deviations of 10. Higher scores indicate better health-related QoL. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Week 48/ET visit

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Physical component score, Week 48/ET (n=57, 83)	-1.47 (± 7.17)	4.47 (± 11.06)		
Mental Component Score, Week 48/ET (n=57, 83)	-1.88 (± 9.05)	3.07 (± 11.53)		
Physical Functioning Domain, Week 48/ET (n=57, 83)	-1.8 (± 7.5)	3.49 (± 10.74)		
Role Physical Domain, Week 48/ET (n=57, 83)	-1.38 (± 7.87)	4.6 (± 12.62)		
Bodily Pain Domain, Week 48/ET (n=57, 83)	-1.6 (± 7.9)	6.15 (± 12.92)		
General Health Domain, Week 48/ET (n=57, 83)	-1.42 (± 10)	2.25 (± 7.99)		

Vitality Domain, Week 48/ET (n=57, 83)	-1.63 (± 10.39)	4.47 (± 12.16)		
Social Functioning Domain, Week 48/ET (n=57, 83)	-2.92 (± 9.09)	3.69 (± 13.46)		
Role Emotional Domain, Week 48/ET (n=57, 82)	-2.26 (± 10.29)	3.28 (± 11.38)		
Mental Health Domain, Week 48/ET (n=57, 83)	-1.02 (± 8.63)	2.87 (± 11.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL 5 Dimensions Questionnaire (EQ-5D) Utility Scores at Baseline and Week 48/ET Visit

End point title	EuroQoL 5 Dimensions Questionnaire (EQ-5D) Utility Scores at Baseline and Week 48/ET Visit
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End point description:

EQ5D 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, selfcare, 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. n = number of participants with non-missing data.

End point type	Secondary
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End point timeframe:

Baseline and Week 48/ET visit

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Utility Score, Baseline (n=62, 85)	0.85 (± 0.21)	0.57 (± 0.28)		
Utility Score, Week 48/ET (n=57, 83)	0.84 (± 0.16)	0.66 (± 0.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline EQ-5D Utility Scores at Week 48/ET Visit

End point title	Change from Baseline EQ-5D Utility Scores at Week 48/ET Visit
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End point description:

EQ5D 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, selfcare, 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.

End point type	Secondary
End point timeframe:	
Baseline and Week 48/ET visit	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	83		
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.02 (± 0.21)	0.1 (± 0.36)		

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
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End point description:

EQ5D 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. n = number of participants with non-missing data.

End point type	Secondary
End point timeframe:	
Baseline and Week 48/ET visit	

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Score on a scale				
arithmetic mean (standard deviation)				
VAS Score, Baseline (n=62, 86)	77.98 (± 16.18)	48.6 (± 19.21)		
VAS Score, Week 48/ET (n=57, 83)	73.4 (± 18.54)	57.6 (± 24.6)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline EQ-5D VAS Scores at Week 8/ET Visit
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End point description:

EQ5D 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 mm (worst imaginable health state) to 100 mm (best imaginable health state); higher scores indicate a better health state.

End point type	Secondary
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End point timeframe:

Baseline and Week 48/ET visit

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	83		
Units: Score on a scale				
arithmetic mean (standard deviation)	-3.79 (± 20.56)	10.16 (± 26.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Hospitalized Due to Crohn's Disease

End point title	Percentage of Participants Hospitalized Due to Crohn's Disease
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End point description:

The number of participants hospitalized due to Crohn's disease were recorded at every study visit.

End point type	Secondary
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End point timeframe:

From baseline to Week 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Percentage of participants				
number (not applicable)	11.3	15.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Hospitalizations Due to Crohn's Disease

End point title	Length of Hospitalizations Due to Crohn's Disease
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End point description:

The length of hospitalizations due to Crohn's disease were recorded at every study visit.

End point type	Secondary
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End point timeframe:

From baseline to Week 52/follow-up

End point values	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	88		
Units: Percentage of participants				
number (not applicable)				
<3 days	1.6	2.3		
3 to 6 days	6.5	10.2		
7 to 10 days	0	3.4		
> 10 days	0	3.4		

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. Non-SAEs were recorded from time of first dose of study treatment through last participant visit.

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	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Tofacitinib 5 mg BID
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Reporting group description:

Tofacitinib 5 mg tablet for oral administration at a dose of 5 mg BID for up to 48 weeks.

Reporting group title	Tofacitinib 10 mg BID
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Reporting group description:

Tofacitinib 10 mg tablets (2 x 5 mg tablets) for oral administration at a dose of 10 mg BID for up to 48 weeks.

Serious adverse events	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 62 (8.06%)	14 / 88 (15.91%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colon dysplasia			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	3 / 62 (4.84%)	7 / 88 (7.95%)	
occurrences causally related to treatment / all	0 / 3	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Perineal fistula			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 88 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			

subjects affected / exposed	0 / 62 (0.00%)	1 / 88 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 62 (67.74%)	58 / 88 (65.91%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 62 (3.23%)	2 / 88 (2.27%)	
occurrences (all)	2	2	
Cyst			
subjects affected / exposed	2 / 62 (3.23%)	0 / 88 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	1 / 62 (1.61%)	4 / 88 (4.55%)	
occurrences (all)	1	4	
Pyrexia			
subjects affected / exposed	1 / 62 (1.61%)	6 / 88 (6.82%)	
occurrences (all)	1	7	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed ^[1]	0 / 30 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Balanoposthitis			
subjects affected / exposed ^[2]	1 / 32 (3.13%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction			

<p>subjects affected / exposed^[3]</p> <p>occurrences (all)</p>	<p>1 / 32 (3.13%)</p> <p>1</p>	<p>0 / 47 (0.00%)</p> <p>0</p>	
<p>Oligomenorrhoea</p> <p>subjects affected / exposed^[4]</p> <p>occurrences (all)</p>	<p>0 / 30 (0.00%)</p> <p>0</p>	<p>1 / 41 (2.44%)</p> <p>1</p>	
<p>Testicular swelling</p> <p>subjects affected / exposed^[5]</p> <p>occurrences (all)</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	<p>1 / 47 (2.13%)</p> <p>1</p>	
<p>Vulvovaginal pruritus</p> <p>subjects affected / exposed^[6]</p> <p>occurrences (all)</p>	<p>0 / 30 (0.00%)</p> <p>0</p>	<p>1 / 41 (2.44%)</p> <p>1</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 62 (1.61%)</p> <p>1</p>	<p>2 / 88 (2.27%)</p> <p>2</p>	
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 62 (0.00%)</p> <p>0</p> <p>2 / 62 (3.23%)</p> <p>2</p>	<p>3 / 88 (3.41%)</p> <p>3</p> <p>0 / 88 (0.00%)</p> <p>0</p>	
<p>Investigations</p> <p>Blood alkaline phosphatase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood creatine phosphokinase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>C-reactive protein increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gamma-glutamyltransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 62 (3.23%)</p> <p>2</p> <p>3 / 62 (4.84%)</p> <p>4</p> <p>2 / 62 (3.23%)</p> <p>2</p> <p>2 / 62 (3.23%)</p> <p>2</p>	<p>0 / 88 (0.00%)</p> <p>0</p> <p>5 / 88 (5.68%)</p> <p>5</p> <p>0 / 88 (0.00%)</p> <p>0</p> <p>0 / 88 (0.00%)</p> <p>0</p>	

Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	2 / 88 (2.27%) 8	
Smear cervix abnormal subjects affected / exposed ^[7] occurrences (all)	1 / 30 (3.33%) 1	0 / 41 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	1 / 88 (1.14%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 2	2 / 88 (2.27%) 2	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 62 (4.84%) 5	4 / 88 (4.55%) 4	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0	2 / 88 (2.27%) 2	
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	3 / 88 (3.41%) 3	
Abdominal pain subjects affected / exposed occurrences (all)	7 / 62 (11.29%) 7	7 / 88 (7.95%) 8	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	2 / 88 (2.27%) 2	
Anal fissure subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	2 / 88 (2.27%) 2	
Aphthous ulcer subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	3 / 88 (3.41%) 3	

Constipation		
subjects affected / exposed	2 / 62 (3.23%)	1 / 88 (1.14%)
occurrences (all)	2	1
Crohn's disease		
subjects affected / exposed	19 / 62 (30.65%)	11 / 88 (12.50%)
occurrences (all)	22	13
Diarrhoea		
subjects affected / exposed	3 / 62 (4.84%)	1 / 88 (1.14%)
occurrences (all)	3	1
Dyspepsia		
subjects affected / exposed	0 / 62 (0.00%)	3 / 88 (3.41%)
occurrences (all)	0	6
Flatulence		
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)
occurrences (all)	0	2
Food poisoning		
subjects affected / exposed	2 / 62 (3.23%)	0 / 88 (0.00%)
occurrences (all)	2	0
Haematochezia		
subjects affected / exposed	1 / 62 (1.61%)	2 / 88 (2.27%)
occurrences (all)	1	2
Haemorrhoids		
subjects affected / exposed	0 / 62 (0.00%)	4 / 88 (4.55%)
occurrences (all)	0	4
Nausea		
subjects affected / exposed	2 / 62 (3.23%)	9 / 88 (10.23%)
occurrences (all)	2	9
Proctalgia		
subjects affected / exposed	1 / 62 (1.61%)	2 / 88 (2.27%)
occurrences (all)	1	2
Toothache		
subjects affected / exposed	3 / 62 (4.84%)	0 / 88 (0.00%)
occurrences (all)	3	0
Vomiting		
subjects affected / exposed	1 / 62 (1.61%)	6 / 88 (6.82%)
occurrences (all)	2	6

Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	1 / 62 (1.61%)	2 / 88 (2.27%)	
occurrences (all)	1	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 62 (8.06%)	8 / 88 (9.09%)	
occurrences (all)	6	8	
Back pain			
subjects affected / exposed	1 / 62 (1.61%)	4 / 88 (4.55%)	
occurrences (all)	1	4	
Muscle spasms			
subjects affected / exposed	2 / 62 (3.23%)	2 / 88 (2.27%)	
occurrences (all)	2	2	
Infections and infestations			
Bartholin's abscess			
subjects affected / exposed ^[8]	0 / 30 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Bartholinitis			
subjects affected / exposed ^[9]	0 / 30 (0.00%)	2 / 41 (4.88%)	
occurrences (all)	0	2	
Cystitis			
subjects affected / exposed	2 / 62 (3.23%)	0 / 88 (0.00%)	
occurrences (all)	2	0	
Folliculitis			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	7 / 62 (11.29%)	2 / 88 (2.27%)	
occurrences (all)	7	2	
Herpes zoster			
subjects affected / exposed	1 / 62 (1.61%)	2 / 88 (2.27%)	
occurrences (all)	1	2	

Influenza			
subjects affected / exposed	5 / 62 (8.06%)	8 / 88 (9.09%)	
occurrences (all)	5	9	
Nasopharyngitis			
subjects affected / exposed	8 / 62 (12.90%)	7 / 88 (7.95%)	
occurrences (all)	11	7	
Oral herpes			
subjects affected / exposed	3 / 62 (4.84%)	0 / 88 (0.00%)	
occurrences (all)	3	0	
Pharyngitis			
subjects affected / exposed	2 / 62 (3.23%)	0 / 88 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 62 (3.23%)	2 / 88 (2.27%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	8 / 62 (12.90%)	7 / 88 (7.95%)	
occurrences (all)	14	8	
Vaginal infection			
subjects affected / exposed ^[10]	1 / 30 (3.33%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Vaginitis bacterial			
subjects affected / exposed ^[11]	0 / 30 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed ^[12]	0 / 30 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection			
subjects affected / exposed ^[13]	0 / 30 (0.00%)	2 / 41 (4.88%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	3	
Hypercholesterolaemia			

subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	2	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 62 (0.00%)	2 / 88 (2.27%)	
occurrences (all)	0	2	

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.

[2] - 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 male participants were counted as exposed to this adverse event.

[3] - 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 male participants were counted as exposed to this adverse event.

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

Justification: Only female participants were counted as exposed to this adverse event.

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

Justification: Only male participants were counted as exposed to this adverse event.

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

Justification: Only female participants were counted as exposed to this adverse event.

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

Justification: Only female participants were counted as exposed to this adverse event.

[8] - 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.

[9] - 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.

[10] - 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.

[11] - 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.

[12] - 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.

[13] - 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.

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. This amendment also included an updated prohibited medications table, lymphocyte count requirement for subject selection and monitoring and discontinuation criteria for lymphopenia, guidance regarding surgery during the study, and updates to the Background section among other revisions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported