



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 standard deviation | 41.3 ± 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 |
|-----------------|--|

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-TNF 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.

| | |
|----------------|-----------|
| 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 91 (0.00%) 0 / 0 0 / 0 | 1 / 86 (1.16%) 0 / 1 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 |
| Anal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 91 (0.00%) 0 / 0 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 | 1 / 86 (1.16%) 0 / 1 0 / 0 |
| Cytomegalovirus infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 91 (1.10%) 0 / 1 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 |
| Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 91 (0.00%) 0 / 0 0 / 0 | 1 / 86 (1.16%) 0 / 1 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 |
| Perirectal abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 91 (1.10%) 0 / 1 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 |
| Pneumonia influenzal subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 91 (0.00%) 0 / 0 0 / 0 | 0 / 86 (0.00%) 0 / 0 0 / 0 | 1 / 86 (1.16%) 0 / 1 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 occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 0 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 86 (1.16%) 1 | 2 / 86 (2.33%) 2 |
| 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) | 0 / 91 (0.00%) 0 0 / 91 (0.00%) 0 0 / 91 (0.00%) 0 | 1 / 86 (1.16%) 1 0 / 86 (0.00%) 0 0 / 86 (0.00%) 0 | 2 / 86 (2.33%) 2 0 / 86 (0.00%) 0 0 / 86 (0.00%) 0 |
| Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 2 / 86 (2.33%) 2 | 0 / 86 (0.00%) 0 |
| Cardiac disorders Bradycardia subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 3 / 91 (3.30%) 3 7 / 91 (7.69%) 9 | 1 / 86 (1.16%) 1 8 / 86 (9.30%) 8 | 2 / 86 (2.33%) 3 5 / 86 (5.81%) 5 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy | 1 / 91 (1.10%) 1 | 4 / 86 (4.65%) 4 | 2 / 86 (2.33%) 2 |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 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 occurrences (all) | 1 / 91 (1.10%) 1 | 2 / 86 (2.33%) 2 | 2 / 86 (2.33%) 2 |
| Nausea subjects affected / exposed occurrences (all) | 8 / 91 (8.79%) 8 | 5 / 86 (5.81%) 5 | 7 / 86 (8.14%) 7 |
| Stomatitis subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 1 / 86 (1.16%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 4 / 86 (4.65%) 4 | 5 / 86 (5.81%) 5 |
| Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Night sweats subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 2 / 91 (2.20%) 2 | 2 / 86 (2.33%) 2 | 0 / 86 (0.00%) 0 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 0 / 86 (0.00%) 0 |
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 86 (1.16%) 1 | 2 / 86 (2.33%) 2 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 91 (2.20%) 3 | 2 / 86 (2.33%) 2 | 2 / 86 (2.33%) 2 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 86 (0.00%) 0 | 2 / 86 (2.33%) 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 occurrences (all) | 0 / 16 (0.00%) 0 | | |
| Stomatitis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | | |
| Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Skin and subcutaneous tissue disorders Night sweats subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Rash subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | | |
| Joint swelling subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 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