



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A3921288 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03281304 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

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

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

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

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

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

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

Arm description:

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

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

Dosage and administration details:

Subjects received tofacitinib 5 mg tablet orally BID.

| | |
|------------------|-----------------------|
| Arm title | Tofacitinib 10 mg BID |
|------------------|-----------------------|

Arm description:

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

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

Dosage and administration details:

Subjects received tofacitinib 10 mg tablet orally BID.

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

Period 2

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

Arms

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

Arm description:

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

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

Dosage and administration details:

Subjects received tofacitinib 5 mg tablet orally BID.

| | |
|------------------|-----------------------|
| Arm title | Tofacitinib 10 mg BID |
|------------------|-----------------------|

Arm description:

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

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

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

Dosage and administration details:

Subjects received tofacitinib 10 mg tablet orally BID.

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

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Tofacitinib 5 mg BID |
|-----------------------|----------------------|

Reporting group description:

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

| | |
|-----------------------|-----------------------|
| Reporting group title | Tofacitinib 10 mg BID |
|-----------------------|-----------------------|

Reporting group description:

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

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

End points

End points reporting groups

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

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

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

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

Statistical analyses

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

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

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

| | |
|--|--|
| End point title | Time to Loss of Remission Based on Modified Mayo Score Using Kaplan-Meier Method |
| End point description: | |
| Time to loss of remission(flare):time from first drug administration until time of meeting loss of remission criteria based on modified mayo score(MMS). Loss of remission: meeting ≥ 1 criteria: increase from Baseline in rectal bleeding subscore by ≥ 1 point, increase in endoscopic subscore by ≥ 1 point; increase from Baseline in rectal bleeding subscore by ≥ 2 points, endoscopic subscore >0 ; increase in stool frequency subscore by ≥ 2 points, increase in endoscopic subscore by ≥ 1 point; increase in endoscopic subscore by ≥ 2 points. MMS included 3 components: stool frequency, rectal bleeding and endoscopic subscores, each subscore graded from 0 to 3 with higher scores for each score=more severe disease. All scores summed up to give total modified mayo score range from 0 to 9; higher scores=more severe disease. FAS: all subjects who were randomised and received at least 1 dose of IP. 999=Median was not estimated due to insufficient number of subjects with event. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Month 42 | |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

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

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

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

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

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

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

Statistical analysis description:

Month 12: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 15.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.2 |
| upper limit | 28.7 |

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

Statistical analysis description:

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

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 14.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 28.5 |

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

Statistical analysis description:

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

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
|-------------------|--|

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

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

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

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

Statistical analysis description:

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

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

Statistical analysis title

Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

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

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

Statistical analysis title

Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

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

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

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

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

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 6, 18, 30 and 42

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

Statistical analyses

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

Statistical analysis description:

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

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
|-------------------|--|

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

| | |
|--|---|
| Statistical analysis title | Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID |
| Statistical analysis description: Month 18: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 20 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.6 |
| upper limit | 35 |

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

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

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

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

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

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

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

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

Statistical analysis description:

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

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

Statistical analysis title

Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

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

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

Statistical analysis title

Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID

Statistical analysis description:

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

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

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

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

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

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

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

Statistical analysis description:

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

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

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

Statistical analysis description:

Month 36: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

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

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

Statistical analysis description:

Month 39: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
|-------------------|--|

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

| | |
|--|---|
| Statistical analysis title | Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID |
| Statistical analysis description: Month 42: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 2.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13 |
| upper limit | 18.5 |

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

| | |
|--|--|
| End point title | Number of Subjects With Remission Based on Modified Mayo Score at Months 18, 30 and 42 |
| End point description: Remission as per modified mayo score was defined as an endoscopic subscore of 0 or 1, stool frequency subscore of 0 or 1, and rectal bleeding subscore of 0. Modified mayo score consisted of 3 components: stool frequency subscore, rectal bleeding subscore and endoscopic subscore: higher scores for each score = more severe disease. These scores were summed up to give a total modified mayo score range of 0 to 9; where higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: Months 18, 30 and 42 | |

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

Statistical analyses

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

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

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

Statistical analysis description:

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

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

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

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

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

Statistical analyses

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Months 18, 30 and 42

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Months 1, 3 and 6

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

Statistical analyses

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

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

| | |
|--|---|
| | Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID |
|--|---|

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

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

| | |
|------------------------|---|
| End point title | Change From Baseline in Modified Partial Mayo Score at Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42 |
| End point description: | Modified partial mayo scores consisted of 2 subscores: stool frequency and rectal bleeding with each subscore graded from 0 to 3 with higher scores indicating more severe disease. Individual subscores were summed up to give a total modified partial mayo score range from 0 (normal or inactive disease) to 6 (severe disease) with higher scores indicating more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. Here, 'Number of Subjects Analysed' =subjects evaluable for this endpoint and n= number of subjects evaluable for each specified time point. |
| End point type | Secondary |
| End point timeframe: | Baseline, Months 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39 and 42 |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6

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

Statistical analyses

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Months 18, 30 and 42

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Months 1, 3 and 6

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

Statistical analyses

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

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

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

Statistical analysis description:

Month 3

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

| | | | | |
|-------------------------------|------------------|------------------|--|--|
| Change at Month 42 (n= 26,25) | 0.1 (\pm 0.5) | 0.2 (\pm 1.1) | | |
|-------------------------------|------------------|------------------|--|--|

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | Number of Subjects With Mucosal Healing at Months 6, 18, 30 and 42 |
| End point description: Mucosal healing in subjects was defined as the mayo endoscopic subscore of 0 or 1. The Mayo endoscopic subscore consisted of the findings of centrally read flexible sigmoidoscopy, graded from 0 to 3 with higher scores indicated more severe disease. FAS included all subjects who were randomised and received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: Months 6, 18, 30 and 42 | |

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

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Tofacitinib 10 mg BID versus Tofacitinib 5 mg BID |
| Statistical analysis description: Month 6: Adjusted (weighted) difference and its 95% CI based on normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 11.4 |

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

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

Statistical analysis description:

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

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 18.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.5 |
| upper limit | 32.6 |

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

Statistical analysis description:

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

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted (weighted) difference |
| Point estimate | 12.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 28.1 |

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

Statistical analysis description:

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

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
|-------------------|--|

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 6, 18, 30 and 42

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

Statistical analyses

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

Statistical analysis description:

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

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID v Tofacitinib 10 mg BID |
|-------------------|--|

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

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|---|
| End point title | Number of Subjects With Treatment Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs) |
| End point description: An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; medically important events. A treatment emergent AE (TEAE) was defined as an event that emerged during the treatment period that was absent before treatment or worsened during the treatment period relative to the pretreatment state. AEs included both serious and all non-serious adverse events (irrespective of frequency threshold used to report other AEs in safety section). Safety analysis set (SAS) included all subjects who received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: Baseline up to 43 months | |

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Infections

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

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 43 months | |

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Laboratory Abnormalities

| | |
|---|---|
| End point title | Number of Subjects With Clinical Laboratory Abnormalities |
| End point description: | |
| Abnormality criteria: Haematology: haemoglobin(Hg):<0.8* lower limit of normal(LLN); haematocrit:<0.8*LLN; lymphocytes:<0.8*LLN; lymphocytes/leukocytes: <0.8*LLN; erythrocytes(ery.):<0.8*LLN; ery. mean corpuscular volume: <0.9*LLN; ery. mean corpuscular Hg: <0.9*LLN; reticulocytes, reticulocytes/ery.:>1.5*upper limit of normal(ULN); neutrophils, neutrophils/leukocytes: >1.2*ULN; basophils/leukocytes, eosinophils, eosinophils/leukocytes, monocytes/leukocytes: >1.2*ULN; leukocyte esterase: >=1; Clinical chemistry: bicarbonate:<0.9*LLN, bilirubin(bil): >1.5*ULN; indirect bil: >1.5*ULN; aspartate aminotransferase(AT): >3.0*ULN; alanine AT: >3.0*ULN; gamma glutamyl transferase: >3.0*ULN; creatine kinase: >2.0*ULN; potassium: >1.1*ULN; blood urea nitrogen: >1.3*ULN; creatinine: >1.3*ULN; urate: >1.2*ULN; cholesterol: >1.3*ULN; HDL-cholesterol: <0.8*LLN; LDL-cholesterol: >1.2*ULN; triglycerides: >1.3*ULN; glucose: >1.5*ULN; urine Hg:>=1. SAS:all subjects who received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 27 months | |

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

Statistical analyses

No statistical analyses for this end point

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

| | | | | |
|-----------------|---|--|--|--|
| End point title | Number of Subjects With Clinically Significant Laboratory | | | |
|-----------------|---|--|--|--|

End point description:

Laboratory abnormalities leading to study treatment discontinuation: 2 sequential neutrophil counts <750 neutrophils per cubic millimeter (mm³); 2 sequential lymphocyte counts <500 lymphocytes/mm³; 2 sequential hemoglobin <8.0 grams per deciliter; 2 sequential platelet counts <75000 platelets/mm³; 2 sequential AST or ALT elevations $\geq 3 \times \text{ULN}$ with at least one total bilirubin value $\geq 2 \times \text{ULN}$; 2 sequential AST or ALT elevations $\geq 3 \times \text{ULN}$ accompanied by signs or symptoms consistent with hepatic injury; 2 sequential AST or ALT elevations $\geq 5 \times \text{ULN}$; 2 sequential increases in creatinine >50% and >0.5 milligrams per deciliter over A3921139 baseline; 2 sequential CK elevations >10*ULN unless the causality is known not to be medically serious (eg, exercise induced). SAS: all subjects who received at least 1 dose of IP.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline up to 43 months

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Sign Abnormalities

| | |
|-----------------|--|
| End point title | Number of Subjects With Vital Sign Abnormalities |
|-----------------|--|

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline up to 43 months

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

| | | | | |
|------------------------------------|---|---|--|--|
| SBP: Change \geq 30mmHg decrease | 6 | 6 | | |
|------------------------------------|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Physical Examinations Abnormalities

| | |
|---|--|
| End point title | Number of Subjects With Clinically Significant Physical Examinations Abnormalities |
| End point description: Physical examination included assessment of the weight, general appearance, eyes, mouth, lungs, heart, abdomen, musculoskeletal, extremities, skin and lymph nodes. Clinical significance was assessed by the investigator. SAS included all subjects who received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: Baseline up to 43 months | |

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | Number of Subjects With Opportunistic Infections, all Malignancy, Gastrointestinal Perforation and Cardiovascular Events Adjudicated by Adjudication Committee |
| End point description: Number of subjects with adjudicated opportunistic infections including herpes zoster (non-adjacent or >2 adjacent dermatomes); all malignancies including non-melanoma skin cancer; gastrointestinal perforation and cardiovascular events including pulmonary embolism and cerebrovascular accident, adjudicated by adjudication committee were reported. SAS included all subjects who received at least 1 dose of IP. | |
| End point type | Secondary |
| End point timeframe: Baseline up to 43 months | |

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 43 months

Adverse event reporting additional description:

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

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Tofacitinib 10 mg BID |
|-----------------------|-----------------------|

Reporting group description:

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

| | |
|-----------------------|----------------------|
| Reporting group title | Tofacitinib 5 mg BID |
|-----------------------|----------------------|

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

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

Notes:

Limitations and caveats

None reported