# Clinical trial results:
# A Multi-center, Open-Label Study of CP-690,550 in Subjects With Moderate to Severe Ulcerative Colitis

## Summary

| | |
|---|---|
| EudraCT number | 2011-004581-14 |
| Trial protocol | CZ DK HU EE GB LV BE NL ES AT DE SK PL IT HR |
| Global end of trial date | 06 August 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 August 2021 |
| First version publication date | 19 August 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | A3921139 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01470612 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

### Paediatric regulatory details

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

Notes:

### Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 16 March 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 August 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety and tolerability of long-term tofacitinib therapy in subjects with ulcerative colitis (UC).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for 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 | 01 October 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 30 |
| Country: Number of subjects enrolled | Brazil: 2 |
| Country: Number of subjects enrolled | Canada: 28 |
| Country: Number of subjects enrolled | Colombia: 2 |
| Country: Number of subjects enrolled | Israel: 6 |
| Country: Number of subjects enrolled | Japan: 53 |
| Country: Number of subjects enrolled | Korea, Republic of: 51 |
| Country: Number of subjects enrolled | New Zealand: 29 |
| Country: Number of subjects enrolled | Russian Federation: 33 |
| Country: Number of subjects enrolled | Serbia: 34 |
| Country: Number of subjects enrolled | South Africa: 26 |
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | Ukraine: 47 |
| Country: Number of subjects enrolled | United States: 166 |
| Country: Number of subjects enrolled | Austria: 30 |
| Country: Number of subjects enrolled | Belgium: 61 |
| Country: Number of subjects enrolled | Croatia: 1 |
| Country: Number of subjects enrolled | Denmark: 14 |
| Country: Number of subjects enrolled | Estonia: 8 |
| Country: Number of subjects enrolled | France: 29 |
| Country: Number of subjects enrolled | Germany: 50 |
| Country: Number of subjects enrolled | Hungary: 32 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | Latvia: 1 |
| Country: Number of subjects enrolled | Netherlands: 32 |
| Country: Number of subjects enrolled | Poland: 56 |
| Country: Number of subjects enrolled | Romania: 9 |

| | |
|---|---|
| Country: Number of subjects enrolled | Slovakia: 33 |
| Country: Number of subjects enrolled | Spain: 21 |
| Country: Number of subjects enrolled | Czechia: 15 |
| Country: Number of subjects enrolled | United Kingdom: 21 |
| Worldwide total number of subjects | 944 |
| EEA total number of subjects | 415 |

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) | 881 |
| From 65 to 84 years | 63 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects enrolled in this Study A3921139: 1) who had completed or had early withdrawal due to treatment failure in Study A3921096 (NCT01458574) 2) or who were non-responders after completing induction studies A3921094 (NCT01465763) or A3921095 (NCT01458951). Eligible participants were assigned to either Tofacitinib 5 mg BID or 10 mg BID group.

### Pre-assignment

Screening details:

Treatment failure for A3921096: Increase in Mayo score of >=3 points from baseline and rectal bleeding sub score by >=1 point and endoscopic sub score of >=1 point post minimum of 8 weeks treatment. If endoscopic sub score and baseline endoscopic sub score was 3 (maximum), then increase by >=1 point was not needed, but all other criteria must met.

### Period 1

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

### Arms

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

Arm description:

Subjects who completed Study A3921096 and were in remission at Week 52 of Study A3921096, received Tofacitinib 5 milligram (mg) tablets twice daily (BID) for maximum of 80 months in this Study A3921139. Remission was defined as total Mayo score less than or equal to (<=) 2 with no individual sub score greater than (>)1 and rectal bleeding sub score of 0.

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

Dosage and administration details:

Subjects received Tofacitinib 5 mg tablets orally twice daily.

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

Arm description:

Subjects who had completed Study A3921096 and not in remission, or who had early withdrawal due to treatment failure from Study A3921096, or who were non responders after completing A3921094 or A3921095 received Tofacitinib 10 mg tablets twice daily for maximum of 84 months in this Study A3921139.

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

Dosage and administration details:

Subjects received Tofacitinib 10 mg tablets orally twice daily.

| **Number of subjects in period 1** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID |
|---|---|---|
| Started | 175 | 769 |
| Completed | 91 | 104 |
| Not completed | 84 | 665 |
| Protocol deviation | 2 | 7 |
| Lack of efficacy | 20 | 326 |
| Pregnancy | 2 | 10 |
| Adverse event, serious fatal | - | 1 |
| Adverse event, non-fatal | 20 | 80 |
| Did not meet entrance criteria | - | 1 |
| Unspecified | 14 | 156 |
| Consent withdrawn by subject | 24 | 79 |
| Lost to follow-up | 2 | 5 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Tofacitinib 5 mg BID |
| Reporting group description: | |
| Subjects who completed Study A3921096 and were in remission at Week 52 of Study A3921096, received Tofacitinib 5 milligram (mg) tablets twice daily (BID) for maximum of 80 months in this Study A3921139. Remission was defined as total Mayo score less than or equal to (<=) 2 with no individual sub score greater than (>)1 and rectal bleeding sub score of 0. | |
| Reporting group title | Tofacitinib 10 mg BID |
| Reporting group description: | |
| Subjects who had completed Study A3921096 and not in remission, or who had early withdrawal due to treatment failure from Study A3921096, or who were non responders after completing A3921094 or A3921095 received Tofacitinib 10 mg tablets twice daily for maximum of 84 months in this Study A3921139. | |

| Reporting group values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | Total |
|---|---|---|---|
| Number of subjects | 175 | 769 | 944 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 161 | 720 | 881 |
| From 65-84 years | 14 | 49 | 63 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 44.5 | 40.5 | |
| standard deviation | ± 14.6 | ± 13.5 | - |
| Sex: Female, Male<br>Units: subjects | | | |
| Female | 79 | 310 | 389 |
| Male | 96 | 459 | 555 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| White | 136 | 615 | 751 |
| Black | 0 | 9 | 9 |
| Asian | 25 | 97 | 122 |
| Other | 9 | 24 | 33 |
| Unspecified | 5 | 24 | 29 |

## End points

### End points reporting groups

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

Reporting group description:

Subjects who completed Study A3921096 and were in remission at Week 52 of Study A3921096, received Tofacitinib 5 milligram (mg) tablets twice daily (BID) for maximum of 80 months in this Study A3921139. Remission was defined as total Mayo score less than or equal to (<=) 2 with no individual sub score greater than (>)1 and rectal bleeding sub score of 0.

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

Reporting group description:

Subjects who had completed Study A3921096 and not in remission, or who had early withdrawal due to treatment failure from Study A3921096, or who were non responders after completing A3921094 or A3921095 received Tofacitinib 10 mg tablets twice daily for maximum of 84 months in this Study A3921139.

### Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)[1] |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug 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. Treatment-emergent were events between first dose of study drug and up to 81 months for Tofacitininb 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious AEs. Safety analysis set (SAS) included all subjects who received at least 1 dose of study medication in this study.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Subject with AEs | 154 | 626 | | |
| Subject with SAEs | 39 | 147 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Serious Infections as Treatment Emergent Adverse Events (TEAEs)

| End point title | Number of Subjects With Serious Infections as Treatment Emergent Adverse Events (TEAEs)[2] |
|---|---|

End point description:

Serious infections were treated infections that required parenteral antimicrobial therapy or hospitalization for treatment or; met other criteria that required the infection to be classified as a serious adverse event (SAE). 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. Treatment-emergent were events between first dose of study drug and up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group that were absent before treatment or that worsened relative to pretreatment state. SAS included all subjects who received at least 1 dose of study medication in this study.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | 8 | 31 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Laboratory Test Abnormalities

| End point title | Number of Subjects With Laboratory Test Abnormalities[3] |
|---|---|

End point description:

Laboratory abnormalities: Hb, hematocrit, RBC: <0.8*LLN; reticulocytes (absolute [Abs], %):<0.5*LLN,>1.5*ULN;
MCV,MCH:<0.9*LLN,>1.1*ULN;platelets:<0.5*LLN,>1.75*ULN;WBC:<0.6*LLN,>1.5*ULN;lymphocytes (Abs,%), total neutrophils(Abs,%):<0.8*LLN,>1.2* ULN;Basophils(Abs,%),eosinophils(Abs,%),monocytes(Abs,%):>1.2*ULN; total bilirubin,direct and indirect bilirubin:>1.5* ULN;AST,ALT,gamma GT,LDH,ALP:>3.0* ULN;total protein,albumin:<0.8* LLN,>1.2*ULN:BUN,creatinine: >1.3*ULN;uric acid:>1.2*ULN;cholesterol,triglycerides:>1.3*ULN;cholesterol (HDL: <0.8*LLN;LDL:>1.2*ULN);sodium:<0.95*LLN,>1.05*ULN;potassium,chloride,calcium,bicarbonate:<0.9 *LLN, >1.1*ULN; glucose: <0.6*LLN; creatine kinase >2.0*ULN; urine specific gravity: <1.003; urine pH: <4.5; urine (glucose,protein,blood,nitrite,leukocyte,esterase): >=1; Urine (RBC,WBC):>=20;urine

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 761 | | |
| Units: subjects | 162 | 670 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects With Vital Sign Abnormalities

| End point title | Number of Subjects With Vital Sign Abnormalities[4] |
|---|---|

End point description:

Vital sign abnormalities included >=30 millimeter of mercury [mmHg] increase in systolic blood pressure (BP), >=30 mmHg decrease in systolic BP, Systolic BP (<90 mmHg), >=20 mmHg increase in diastolic BP, >=20 mmHg decrease in diastolic BP, diastolic BP (<50 mmHg), pulse rate (<40 beats per minute [BPM]), pulse rate (>120 BPM). SAS included all subjects who received at least 1 dose of study medication in this study. Here, "Number of subjects analysed" signifies subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified category.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 763 | | |
| Units: subjects | | | | |
| Systolic BP (>=30 mmHg increase) (n=172, 748) | 20 | 113 | | |
| Systolic BP (>=30 mmHg decrease) (n=172, 748) | 19 | 44 | | |
| Systolic BP (<90 mmHg) (n=175, 763) | 3 | 13 | | |
| Diastolic BP (>=20 mmHg increase) (n=172, 748) | 21 | 137 | | |
| Diastolic BP (>=20 mmHg decrease) (n=172, 748) | 37 | 78 | | |
| Diastolic BP (<50 mmHg) (n=175, 763) | 3 | 16 | | |
| Pulse Rate (<40 BPM) (n=175, 763) | 1 | 0 | | |
| Pulse Rate (>120 BPM) (n=175, 763) | 0 | 8 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects With Clinically Significant Changes in Physical

## Examinations From Baseline

| End point title | Number of Subjects With Clinically Significant Changes in Physical Examinations From Baseline[5] |
|---|---|

End point description:

Physical examinations included weight, general appearance, head, ears, eyes, nose, mouth, throat, thyroid, skin (presence of rash), lungs (auscultation), heart (auscultation for presence of murmurs, gallops, rubs, peripheral edema), abdominal (palpation and auscultation), perianal, musculoskeletal, extremities, neurologic (mental status, gait, reflexes, motor and sensory function, coordination) and lymph nodes. Clinically significant changes were judged by the investigator. SAS included all subjects who received at least 1 dose of study medication in this study.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | 84 | 391 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Electrocardiogram (ECG) Abnormalities

| End point title | Number of Subjects With Electrocardiogram (ECG) Abnormalities[6] |
|---|---|

End point description:

ECG abnormalities criteria: maximum PR interval (>=300 millisecond); maximum QRS complex (>=200 millisecond); and maximum QT interval (>=500 millisecond). SAS included all subjects who received at least 1 dose of study medication in this study. Here, "Number of subjects analyzed" signifies number of subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified category.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 158 | 707 | | |
| Units: subjects | | | | |
| Maximum PR interval (>=300) (n=157,706) | 0 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Maximum QRS complex (>=200)(n=158,707) | 0 | 0 | | |
| Maximum QT interval (>=500)(n=158,707) | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Incidence Rates for Adjudicated Cardiovascular, Malignancy, Opportunistic Infections and Thromboembolic Safety Events

| End point title | Incidence Rates for Adjudicated Cardiovascular, Malignancy, Opportunistic Infections and Thromboembolic Safety Events[7] |
|---|---|

End point description:

Incidence rates (number of subjects with events per 100 subjects-years) for adjudicated cardiovascular (major adverse cardiovascular event [MACE]), malignancy (non-melanoma skin cancer [NMSC], malignancy excluding NMSC, opportunistic infections (OIs) (both herpes zoster and non herpes zoster OIs) and thromboembolic events (venous thromboembolism) safety events was analyzed.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: Incidence rate | | | | |
| number (confidence interval 95%) | | | | |
| MACE | 0.31 (0.04 to 1.13) | 0.11 (0.01 to 0.40) | | |
| NMSC | 0.96 (0.35 to 2.08) | 0.68 (0.35 to 1.19) | | |
| Malignancies excluding NMSC | 1.09 (0.44 to 2.25) | 1.00 (0.60 to 1.59) | | |
| Herpes Zoster OI | 0.47 (0.10 to 1.37) | 0.79 (0.43 to 1.32) | | |
| Non Herpes Zoster OI | 0.16 (0.00 to 0.87) | 0.17 (0.03 to 0.49) | | |
| Venous thromboembolism | 0.00 (0.00 to 0.57) | 0.33 (0.12 to 0.73) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Remission at Months 2, 12, 24 and 36: Observed Cases

| End point title | Number of Subjects in Remission at Months 2, 12, 24 and 36: Observed Cases |
|---|---|

End point description:

Remission in subjects was defined as a total Mayo score of less than or equals to (<=) 2, with no individual sub score exceeding 1 point and a rectal bleeding sub score of 0. Mayo score was an instrument designed to measure disease activity of ulcerative colitis (UC). It consisted of 4 sub scores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and physician global assessment (PGA), each sub score graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 12, where higher score indicated more severe disease. FAS included all subjects who received at least 1 dose of study medication in this study. Here, "Number of subjects analysed" signifies subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified timepoint. Data is presented for observed cases, no imputation technique was applied.

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

End point timeframe:

Months 2, 12, 24 and 36

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 164 | 676 | | |
| Units: subjects | | | | |
| Month 2 (n= 164, 676) | 131 | 188 | | |
| Month 12 (n= 154, 447) | 129 | 279 | | |
| Month 24 (n= 132, 371) | 103 | 264 | | |
| Month 36 (n= 113, 299) | 98 | 239 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Remission at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF)

| End point title | Number of Subjects in Remission at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF) |
|---|---|

End point description:

Remission in subjects was defined as a total Mayo score of <=2, with no individual sub score exceeding 1 point and a rectal bleeding sub score of 0. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 sub scores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each sub score graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 12, where higher score indicated more severe disease. FAS included all subjects who received at least 1 dose of study medication in this study. NRI method was used for missing data except for visits after a subject advanced to other studies where LOCF method was used.

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

End point timeframe:

Months 2, 12, 24 and 36

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Month 2 | 131 | 188 | | |
| Month 12 | 129 | 279 | | |
| Month 24 | 103 | 264 | | |
| Month 36 | 103 | 259 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Clinical Remission at Months 2, 12, 24 and 36: Observed Cases

| End point title | Number of Subjects in Clinical Remission at Months 2, 12, 24 and 36: Observed Cases |
|---|---|

End point description:

Clinical remission in subjects was defined as a total mayo score of <=2 with no individual sub score exceeding 1 point. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 sub scores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 12, where higher score indicated more severe disease. Here, "Number of subjects analysed" signifies subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified time point. Data is presented for observed cases, no imputation technique was applied.

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

End point timeframe:

Months 2, 12, 24 and 36

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 164 | 676 | | |
| Units: subjects | | | | |
| Month 2 (n= 164, 676) | 132 | 191 | | |
| Month 12 (n= 154, 447) | 129 | 282 | | |
| Month 24 (n= 132, 371) | 104 | 266 | | |
| Month 36 (n= 113, 299) | 102 | 240 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Clinical Remission at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF)

| End point title | Number of Subjects in Clinical Remission at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF) |
|---|---|

End point description:

Clinical remission in subjects was defined as a total mayo score of <=2 with no individual sub score exceeding 1 point. Mayo score was an instrument designed to measure disease activity of UC. It consisted of 4 sub scores: stool frequency, rectal bleeding, findings of flexible sigmoidoscopy and PGA, each graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 12, where higher score indicated more severe disease. FAS included all subjects who received at least 1 dose of study medication in this study. NRI method was used for missing data except for visits after a subject advanced to other studies where LOCF method was used.

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

End point timeframe:

Months 2, 12, 24 and 36

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Month 2 | 132 | 191 | | |
| Month 12 | 129 | 282 | | |
| Month 24 | 104 | 266 | | |
| Month 36 | 107 | 260 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Subjects in Partial Mayo Score (PMS) Remission at Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84: Observed Cases**

| End point title | Number of Subjects in Partial Mayo Score (PMS) Remission at Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84: Observed Cases |
|---|---|

End point description:

PMS was an instrument designed to measure disease activity of UC without endoscopy. It consisted of 3 sub scores: stool frequency, rectal bleeding and PGA, each sub score graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 9, where higher score indicated more severe disease. PMS remission was defined as a partial Mayo score <=2 with no individual sub score >1. Here, "Number of subjects analysed" signifies subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified timepoint. Data is presented for observed cases, no imputation technique was applied. Here, 99999 indicated data could not be reported as no subjects were evaluable at that time point.

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

End point timeframe:

Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84

| End point values | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 729 | | |
| Units: subjects | | | | |
| Month 1 (n= 165, 729) | 158 | 275 | | |
| Month 4 (n= 165, 532) | 152 | 375 | | |
| Month 6 (n= 166, 505) | 155 | 395 | | |
| Month 9 (n= 160, 469) | 154 | 390 | | |
| Month 15 (n= 145, 418) | 139 | 361 | | |
| Month 18 (n= 144, 404) | 137 | 354 | | |
| Month 21 (n= 138, 394) | 125 | 351 | | |
| Month 27 (n= 125, 348) | 117 | 319 | | |
| Month 30 (n= 124, 338) | 117 | 307 | | |
| Month 33 (n= 118, 326) | 111 | 304 | | |
| Month 39 (n= 105, 281) | 102 | 261 | | |
| Month 42 (n= 100, 253) | 95 | 236 | | |
| Month 45 (n= 102, 226) | 95 | 212 | | |
| Month 48 (n= 92, 199) | 87 | 183 | | |
| Month 51 (n= 89, 175) | 87 | 162 | | |
| Month 54 (n= 71, 147) | 68 | 140 | | |
| Month 57 (n= 56, 128) | 54 | 120 | | |
| Month 60 (n= 39, 107) | 38 | 98 | | |
| Month 63 (n= 28, 89) | 28 | 80 | | |
| Month 66 (n= 89, 175) | 19 | 67 | | |
| Month 69 (n= 11, 54) | 10 | 49 | | |
| Month 72 (n= 6, 44) | 6 | 40 | | |
| Month 75 (n= 3, 26) | 3 | 24 | | |
| Month 78 (n= 4, 19) | 4 | 18 | | |
| Month 81 (n= 0, 11) | 99999 | 10 | | |
| Month 84 (n= 0, 8) | 99999 | 6 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Partial Mayo Score (PMS) Remission at Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF)

| End point title | Number of Subjects in Partial Mayo Score (PMS) Remission at Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF) |
|---|---|

End point description:

PMS was an instrument designed to measure disease activity of UC without endoscopy. It consisted of 3 sub scores: stool frequency, rectal bleeding and PGA, each sub score graded from 0 to 3 with higher scores indicated higher disease severity. These sub scores were summed up to give a total score range of 0 to 9, where higher score indicated more severe disease. PMS remission was defined as a partial Mayo score <=2 with no individual sub score >1. FAS included all subjects who received at least 1 dose of study medication in this study. Here, "n" signifies subjects evaluable at each specified time point. NRI method was used for missing data at all visits except for visits after a participant advanced to other studies and would reach the visits if the subject stayed in the study where LOCF method was used.

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

End point timeframe:

Months 1, 4, 6, 9, 15, 18, 21, 27, 30, 33, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81 and 84

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Month 1 (n= 175, 769) | 158 | 275 | | |
| Month 4 (n= 175, 769) | 152 | 375 | | |
| Month 6 (n= 175, 769) | 155 | 395 | | |
| Month 9 (n= 175, 769) | 154 | 390 | | |
| Month 15 (n= 175, 769) | 139 | 361 | | |
| Month 18 (n= 175, 769) | 137 | 354 | | |
| Month 21 (n= 175, 769) | 125 | 351 | | |
| Month 27 (n= 175, 769) | 117 | 325 | | |
| Month 30 (n= 175, 769) | 117 | 316 | | |
| Month 33 (n= 175, 769) | 114 | 317 | | |
| Month 39 (n= 175, 769) | 108 | 293 | | |
| Month 42 (n= 175, 769) | 102 | 286 | | |
| Month 45 (n= 175, 769) | 102 | 283 | | |
| Month 48 (n= 175, 769) | 95 | 274 | | |
| Month 51 (n= 175, 769) | 96 | 267 | | |
| Month 54 (n= 170, 764) | 76 | 250 | | |
| Month 57 (n= 160, 753) | 61 | 234 | | |
| Month 60 (n= 149, 732) | 44 | 213 | | |
| Month 63 (n= 135, 707) | 31 | 194 | | |
| Month 66 (n= 125, 659) | 22 | 168 | | |
| Month 69 (n= 114, 562) | 13 | 131 | | |
| Month 72 (n= 109, 468) | 7 | 102 | | |
| Month 75 (n= 102, 412) | 3 | 73 | | |
| Month 78 (n= 96, 339) | 4 | 52 | | |
| Month 81 (n= 95, 284) | 0 | 29 | | |
| Month 84 (n= 91, 210) | 0 | 15 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects who Achieved Mucosal Healing at Months 2, 12, 24 and 36: Observed Cases

| End point title | Number of Subjects who Achieved Mucosal Healing at Months 2, 12, 24 and 36: Observed Cases |
|---|---|

End point description:

Mucosal healing in subjects was defined as mayo endoscopic sub score of 0 or 1. The mayo endoscopic sub score consisted of the findings of flexible sigmoidoscopy, graded from 0 to 3 with higher sub scores

indicated higher disease severity. FAS included all subjects who received at least 1 dose of study medication in this study. Here, "Number of subjects analysed" signifies subjects evaluable for this endpoint and "n" signifies subjects evaluable at each specified time point. Data is presented for observed cases, no imputation technique was applied.

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

End point timeframe:

Months 2, 12, 24 and 36

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 169 | 690 | | |
| Units: subjects | | | | |
| Month 2 (n= 169, 690) | 152 | 279 | | |
| Month 12 (n= 156, 458) | 140 | 340 | | |
| Month 24 (n= 136, 382) | 119 | 307 | | |
| Month 36 (n= 115, 307) | 107 | 265 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects who Achieved Mucosal Healing at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF)

| End point title | Number of Subjects who Achieved Mucosal Healing at Months 2, 12, 24 and 36: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF) |
|---|---|

End point description:

Mucosal healing in subjects was defined as mayo endoscopic sub score of 0 or 1. The mayo endoscopic sub score consisted of the findings of flexible sigmoidoscopy, graded from 0 to 3 with higher sub scores indicating higher disease severity. FAS included all subjects who received at least 1 dose of study medication in this study. NRI method was used for missing data at all visits and LOCF method was used for visits after a subject advanced to next study.

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

End point timeframe:

Months 2, 12, 24 and 36

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Month 2 | 152 | 279 | | |
| Month 12 | 140 | 340 | | |
| Month 24 | 119 | 307 | | |
| Month 36 | 113 | 285 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Total Inflammatory Bowel Disease Questionnaire (IBDQ) Score >=170 at Months 2, 6, 12, 18, 24, 30, 36, 48, 60, 72 and 84: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF)

| End point title | Number of Subjects With Total Inflammatory Bowel Disease Questionnaire (IBDQ) Score >=170 at Months 2, 6, 12, 18, 24, 30, 36, 48, 60, 72 and 84: Non-responder Imputation- Last Observation Carried Forward (NRI-LOCF) |
|---|---|

End point description:

IBDQ was a psychometrically validated patient reported outcome (PRO) instrument for measuring the disease-specific quality of life in subjects with inflammatory bowel disease (IBD), including ulcerative colitis consisted of 32 items scored from 1 (worst response) to 7 (best response). For each domain, higher score indicates better quality of life (QOL). Total score was the sum of each item score, and ranged from 32 to 224 with a higher score indicated better QOL. FAS included all subjects who received at least 1 dose of study medication in this study. Here, "n" signifies subjects evaluable at each specified time point. NRI method was used for missing data at all visits except for visits after a subject advanced to other studies and would reach the visits if the subject stayed in the study where LOCF method was used.

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

End point timeframe:

Months 2, 6, 12, 18, 24, 30, 36, 48, 60, 72 and 84

| **End point values** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 769 | | |
| Units: subjects | | | | |
| Month 2 (n= 175, 769) | 154 | 419 | | |
| Month 6 (n= 175, 769) | 151 | 395 | | |
| Month 12 (n= 175, 769) | 140 | 365 | | |
| Month 18 (n= 175, 769) | 123 | 354 | | |
| Month 24 (n= 175, 769) | 120 | 315 | | |
| Month 30 (n= 175, 769) | 115 | 299 | | |
| Month 36 (n= 175, 769) | 111 | 294 | | |
| Month 48 (n= 175, 769) | 93 | 265 | | |
| Month 60 (n= 149, 732) | 45 | 215 | | |
| Month 72 (n= 109, 468) | 8 | 99 | | |
| Month 84 (n= 91, 210) | 0 | 14 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 28 days after last dose of study drug (up to 81 months for Tofacitinib 5 mg BID group and up to 85 months for Tofacitinib 10 mg BID group)

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event. Analysis performed on safety analysis set.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

### Reporting groups

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

Reporting group description:

Subjects who completed Study A3921096 and were in remission at Week 52 of Study A3921096, received Tofacitinib 5 milligram (mg) tablets twice daily (BID) for maximum of 80 months in this Study A3921139. Remission was defined as total Mayo score <=2 with no individual sub score >1 and rectal bleeding sub score of 0.

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

Reporting group description:

Subjects who had completed Study A3921096 and not in remission, or who had early withdrawal due to treatment failure from Study A3921096, or who were non responders after completing A3921094 or A3921095 received Tofacitinib 10 mg tablets twice daily for maximum of 84 months in this Study A3921139.

| **Serious adverse events** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 39 / 175 (22.29%) | 147 / 769 (19.12%) | |
| number of deaths (all causes) | 0 | 6 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Adenocarcinoma metastatic | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Adenocarcinoma of colon | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon adenoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer metastatic | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr virus associated lymphoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |

| | | | |
|---|---|---|---|
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic angiosarcoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leiomyosarcoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Meningioma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to liver | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lymph nodes | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to peritoneum | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |

| | | | |
|---|---|---|---|
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to | 0 / 0 | 1 / 1 | |

| | | | |
|---|---|---|---|
| treatment / all | | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervix haemorrhage uterine | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot fracture | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament rupture | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |

| | | | |
|---|---|---|---|
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to | 0 / 1 | 0 / 0 | |

| | | | |
|---|---|---|---|
| treatment / all | | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 5 / 769 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebellar haemorrhage | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post herpetic neuralgia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |

| | | | |
|---|---|---|---|
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness unilateral | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal skin tags | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 38 / 769 (4.94%) | |
| occurrences causally related to treatment / all | 0 / 4 | 4 / 39 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon dysplasia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |

| | | | |
|---|---|---|---|
| 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 / 175 (0.57%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| 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 | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Megacolon | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prerenal failure | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric obstruction | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acne conglobata | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eosinophilic pustular folliculitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema nodosum | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device loosening | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis reactive | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoroacetabular impingement | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to | 0 / 0 | 0 / 2 | |

| | | | |
|---|---|---|---|
| treatment / all | | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Hyperparathyroidism | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid mass | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Anal abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 3 / 769 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complicated appendicitis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus hepatitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |

| | | | |
|---|---|---|---|
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis infectious | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 4 / 769 (0.52%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster meningitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Histoplasmosis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |

| | | | |
|---|---|---|---|
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastoiditis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis viral | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pulmonary mycosis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 2 / 769 (0.26%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 769 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculosis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 769 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Tofacitinib 5 mg BID | Tofacitinib 10 mg BID | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 134 / 175 (76.57%) | 550 / 769 (71.52%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 17 / 175 (9.71%) | 28 / 769 (3.64%) | |
| occurrences (all) | 18 | 31 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 14 / 769 (1.82%) | |
| occurrences (all) | 4 | 15 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 33 / 769 (4.29%) | |
| occurrences (all) | 6 | 37 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 13 / 769 (1.69%) | |
| occurrences (all) | 4 | 14 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 25 / 769 (3.25%) | |
| occurrences (all) | 2 | 28 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 12 / 769 (1.56%) | |
| occurrences (all) | 5 | 12 | |
| Anxiety | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 16 / 769 (2.08%) | |
| occurrences (all) | 6 | 16 | |
| Insomnia | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 18 / 769 (2.34%) | |
| occurrences (all) | 5 | 19 | |
| Injury, poisoning and procedural complications | | | |
| Skin laceration | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 4 / 769 (0.52%) | |
| occurrences (all) | 5 | 4 | |
| Ligament sprain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 175 (2.29%) | 8 / 769 (1.04%) | |
| occurrences (all) | 4 | 8 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 11 / 769 (1.43%) | |
| occurrences (all) | 6 | 11 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 8 / 769 (1.04%) | |
| occurrences (all) | 5 | 8 | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 7 / 175 (4.00%) | 18 / 769 (2.34%) | |
| occurrences (all) | 7 | 20 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 175 (1.71%) | 18 / 769 (2.34%) | |
| occurrences (all) | 7 | 24 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 8 / 769 (1.04%) | |
| occurrences (all) | 5 | 9 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 19 / 175 (10.86%) | 85 / 769 (11.05%) | |
| occurrences (all) | 22 | 108 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 175 (1.71%) | 36 / 769 (4.68%) | |
| occurrences (all) | 4 | 38 | |
| Lymphopenia | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 13 / 769 (1.69%) | |
| occurrences (all) | 9 | 23 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 14 / 175 (8.00%) | 38 / 769 (4.94%) | |
| occurrences (all) | 19 | 41 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 7 / 769 (0.91%) | |
| occurrences (all) | 5 | 8 | |

| | | | |
|---|---|---|---|
| Rhinorrhoea | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 4 / 769 (0.52%) | |
| occurrences (all) | 4 | 4 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 14 / 769 (1.82%) | |
| occurrences (all) | 4 | 15 | |
| Headache | | | |
| subjects affected / exposed | 12 / 175 (6.86%) | 57 / 769 (7.41%) | |
| occurrences (all) | 23 | 81 | |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 17 / 769 (2.21%) | |
| occurrences (all) | 2 | 17 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 24 / 769 (3.12%) | |
| occurrences (all) | 8 | 33 | |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 47 / 769 (6.11%) | |
| occurrences (all) | 8 | 54 | |
| Constipation | | | |
| subjects affected / exposed | 7 / 175 (4.00%) | 20 / 769 (2.60%) | |
| occurrences (all) | 7 | 20 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 44 / 175 (25.14%) | 131 / 769 (17.04%) | |
| occurrences (all) | 57 | 150 | |
| Dyspepsia | | | |
| subjects affected / exposed | 8 / 175 (4.57%) | 12 / 769 (1.56%) | |
| occurrences (all) | 9 | 12 | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 175 (5.14%) | 34 / 769 (4.42%) | |
| occurrences (all) | 11 | 38 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 10 / 175 (5.71%) | 15 / 769 (1.95%) | |
| occurrences (all) | 11 | 15 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 3 / 175 (1.71%) | 20 / 769 (2.60%) | |

| | | | |
|---|---|---|---|
| occurrences (all) | 3 | 21 | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 175 (1.71%) | 20 / 769 (2.60%) | |
| occurrences (all) | 3 | 23 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 30 / 769 (3.90%) | |
| occurrences (all) | 1 | 37 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 20 / 769 (2.60%) | |
| occurrences (all) | 5 | 22 | |
| Rash | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 38 / 769 (4.94%) | |
| occurrences (all) | 4 | 41 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 11 / 175 (6.29%) | 28 / 769 (3.64%) | |
| occurrences (all) | 16 | 31 | |
| Arthralgia | | | |
| subjects affected / exposed | 17 / 175 (9.71%) | 76 / 769 (9.88%) | |
| occurrences (all) | 22 | 96 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | 18 / 769 (2.34%) | |
| occurrences (all) | 2 | 24 | |
| Myalgia | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 10 / 769 (1.30%) | |
| occurrences (all) | 6 | 12 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | 9 / 769 (1.17%) | |
| occurrences (all) | 6 | 10 | |
| Tendonitis | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 4 / 769 (0.52%) | |
| occurrences (all) | 5 | 4 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 38 / 769 (4.94%) | |
| occurrences (all) | 1 | 43 | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 10 / 769 (1.30%) | |
| occurrences (all) | 4 | 10 | |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 6 / 769 (0.78%) | |
| occurrences (all) | 4 | 6 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 12 / 175 (6.86%) | 51 / 769 (6.63%) | |
| occurrences (all) | 15 | 60 | |
| Bronchitis | | | |
| subjects affected / exposed | 17 / 175 (9.71%) | 30 / 769 (3.90%) | |
| occurrences (all) | 26 | 44 | |
| Herpes zoster | | | |
| subjects affected / exposed | 12 / 175 (6.86%) | 50 / 769 (6.50%) | |
| occurrences (all) | 13 | 52 | |
| Influenza | | | |
| subjects affected / exposed | 23 / 175 (13.14%) | 63 / 769 (8.19%) | |
| occurrences (all) | 32 | 76 | |
| Latent tuberculosis | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 13 / 769 (1.69%) | |
| occurrences (all) | 4 | 13 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 41 / 175 (23.43%) | 157 / 769 (20.42%) | |
| occurrences (all) | 91 | 302 | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 18 / 769 (2.34%) | |
| occurrences (all) | 3 | 42 | |
| Pharyngitis | | | |
| subjects affected / exposed | 8 / 175 (4.57%) | 14 / 769 (1.82%) | |
| occurrences (all) | 8 | 16 | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 175 (2.29%) | 9 / 769 (1.17%) | |

| | | | |
|---|---|---|---|
| occurrences (all) | 5 | 9 | |
| Sinusitis | | | |
| subjects affected / exposed | 8 / 175 (4.57%) | 25 / 769 (3.25%) | |
| occurrences (all) | 13 | 30 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 19 / 175 (10.86%) | 77 / 769 (10.01%) | |
| occurrences (all) | 27 | 114 | |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 7 / 769 (0.91%) | |
| occurrences (all) | 5 | 8 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 13 / 175 (7.43%) | 34 / 769 (4.42%) | |
| occurrences (all) | 20 | 60 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 7 / 769 (0.91%) | |
| occurrences (all) | 5 | 7 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 October 2018 | This amendment specified the end of the trial will be approximately in July 2020. This 2 year extension of the study allowed for additional collection of long term safety and efficacy data in UC patients on tofacitinib. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported